Pam WZ4L (S)
U7
Copy 2

UNIVERSITY OF TORONTO MEDICAL JOURNAL

CARDIOVASCULAR SYSTEM

Editorial		82
Mitral Stenosis	Vera Heller, 5T8	84
Congenital Heart Disease	H. Kleiman, 5T8	91
"On Inspection"	R. C. Bull, 5T8	98
Aortic Insufficiency	Doris E. Kerr, 5T8	100
Essential Hypertension	M. M. Fisher, 5T8	104
Case Report: Dissecting Aneurysm	R. Herst, 5T8	111
Principles of Radiation Hazard Control	J. Hoffman, 5T9	114
Vaginal Bleeding: Part II	P. G. Walfish, 5T8	117
Abstracts	R. F. Armstrong, 5T9	125
Book Reviews		127

JANUARY 1958

VOLUME XXXV NUMBER 3

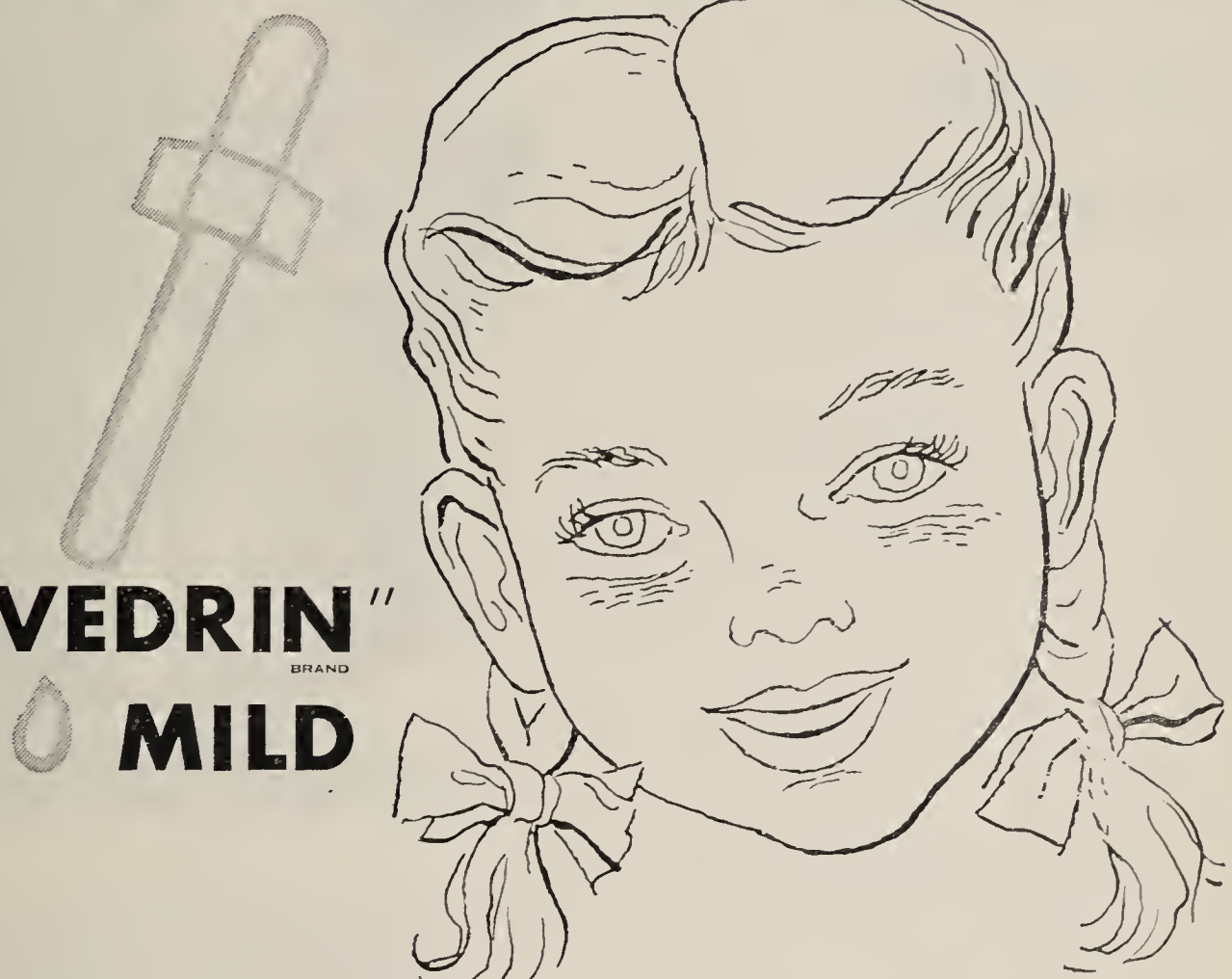
Digitized by the Internet Archive
in 2018 with funding from
University of Toronto

https://archive.org/details/medjournalJan1958uoft

NASAL CONGESTION

in children

quickly relieved



"FLAVEDRIN" BRAND MILD

ANTISEPTIC DECONGESTANT

Dropped or sprayed into the nose, aqueous isotonic Flavedrin provides quick relief and comfort for the patient with a congested running nose. The mucous membrane shrinks, secretion is reduced and ventilation and drainage of accessory sinuses promoted. The antiseptic component is effective against a large number of pathogenic organisms.

"FLAVEDRIN" MILD

Ephedrine hydrochloride..... 0.3%
Aminacrine hydrochloride BP 0.1%

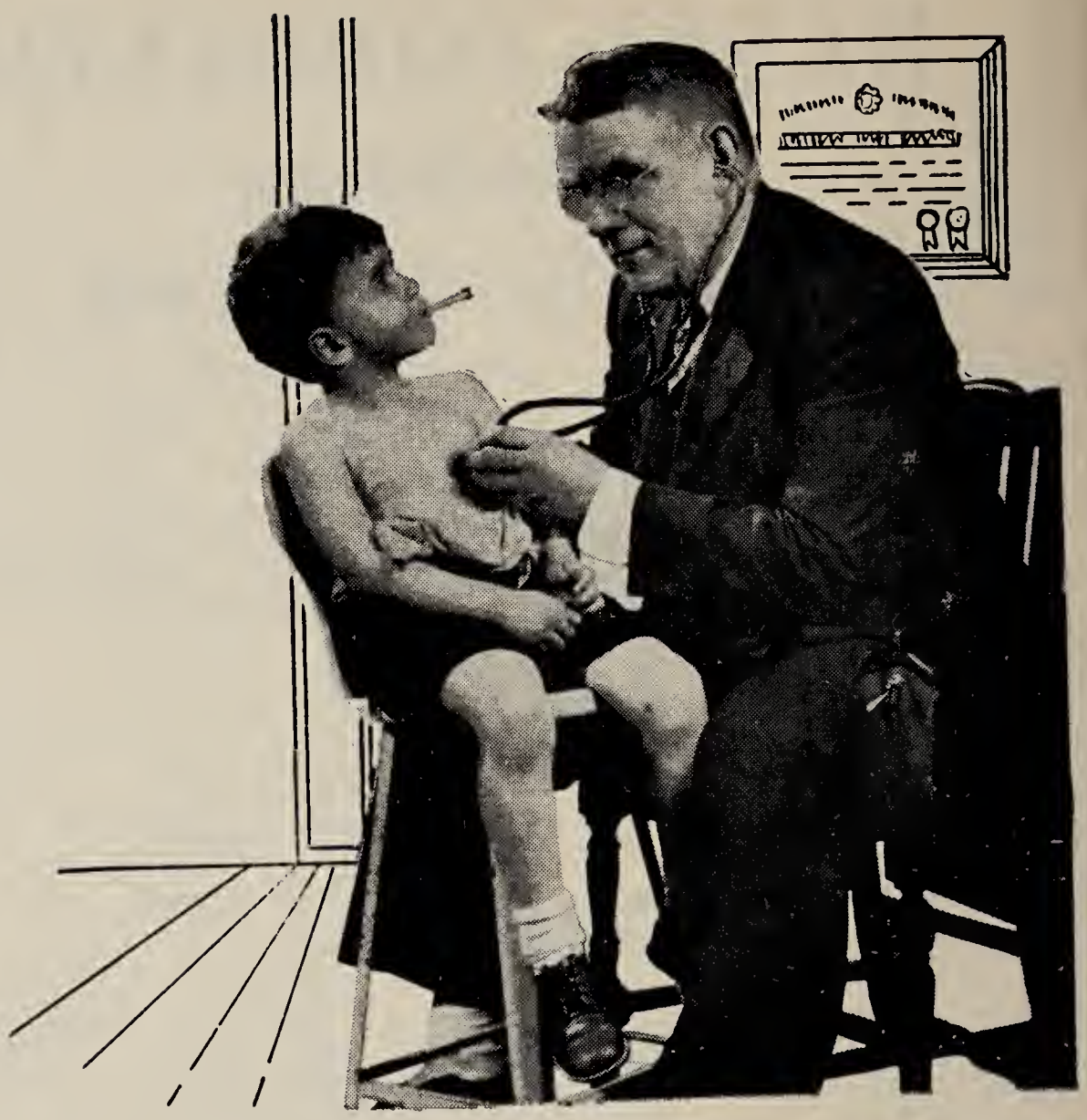
Packaged in ½ oz. bottles with dropper.

ADMINISTRATION: Instil or spray three or four drops into the nostrils every three or four hours.

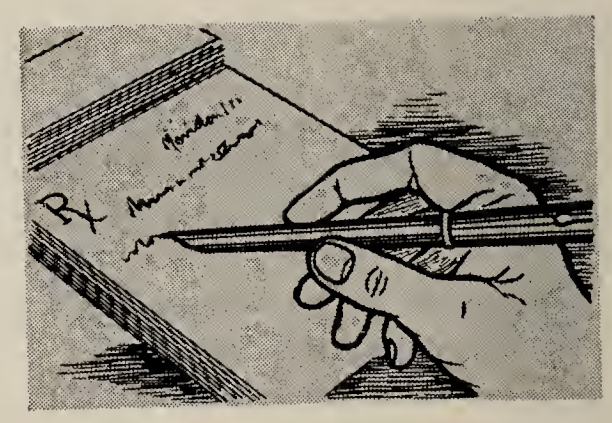
Frosst

Charles E. Frosst & Co.
MONTREAL CANADA

more time for your patients!



▸ when you do this.....



▸ instead of this.....

Let the Pharmacist do ALL your dispensing

By using his resources and abilities, you free yourself of needless detail and expense . . . gaining time to expand your practice.

ONTARIO RETAIL PHARMACISTS ASSOCIATION

THE ONTARIO RETAIL PHARMACISTS' ASSOCIATION

UNIVERSITY OF TORONTO MEDICAL JOURNAL

ESTABLISHED DECEMBER 1923

AN UNDERGRADUATE PUBLICATION

VOLUME XXXV NUMBER 3

TORONTO, JANUARY 1958

Editor-in-Chief ..... A. C. Strickler, 5T8

Associate Editor ..... P. C. F. Moore, 5T9

Assistant Editors: *On Inspection* ..... R. C. Bull, 5T8
Abstracts ..... R. F. Armstrong, 5T9

Business Manager ..... H. P. James, 5T9

Advertising Manager ..... P. B. Dent, 6T0

Circulation Manager ..... D. J. Brand, 6T1

Premedical Representatives ..... G. Boujos, 6T2
Miss W. V. Basser, 6T3

This Journal is published six times a year from November to April, by the Medical Society of the University of Toronto, to serve primarily as a medium for student expression.

Subscription rates: $3.50 for one volume of six consecutive issues. Single copies 65¢.

Manuscripts including references and footnotes should be typewritten double spaced on one side of the paper. References should be kept to a minimum, and should be cited numerically in the order in which they appear in the text.

Manuscripts in excess of 3,000 words will be considered *unsatisfactory.*

Illustrations are included by arrangement with the Editor. Drawings should be done on white paper in black ink.

Final copy date is the first day of *two months* prior to publication, e.g., September 1 for the November issue.

Material printed in this Journal is covered by copyright. Papers are accepted for consideration with the understanding that they are contributed for publication in this Journal only.

Correspondence should be addressed to Room 114, Medical Building, University of Toronto, Toronto 5, Ontario.

Authorized as Second Class Mail, Post Office Department, Ottawa.

EDITORIAL

Why CAMSI?

The Canadian Association of Medical Students and Internes (CAMSI) has three principal aims:

1. To establish and provide basic services for the benefit of all medical students.
2. To prepare medical students for their entrance into practice and resultant medical citizenship.
3. To act as the voice and representative of medical students and internes.

Let us examine each of these aims in turn:

1. CAMSI has established such invaluable services as the Canadian Interne Placement Service (CIPS), a life insurance plan, a hospitalization plan, a film program, free chest X-rays and many others. These have arisen because of student need and student demand; and CAMSI acting as a national body brought them into being. All of us should realize that any unfavourable or neglected aspect of student or interne life is amenable to change, and CAMSI is the vehicle by which such changes can be accomplished.

2. It is all too common for medical students and internes to be very short sighted and take little interest in the world of medicine which they are going to enter after their cloistered days in medical schools and hospitals. Medicine to-day is highly organized in a society which shows strong tendencies toward full socialization. Like it or not, this is the medical atmosphere in which we have to practise.

Organized medicine is not a bad thing—in actual fact, it has produced much good, and it is to our advantage to use the opportunities which it affords. For example, practically all Canadian doctors feel that socialized medicine, which is being so strongly advocated in some quarters, would not provide the high standard of medical care which is available under our present system. By constructive criticism and action, medical organizations have held off irresponsible attempts at socialization of our profession.

Active membership in CAMSI provides undergraduates with an excellent training ground for the complexities of medical practice. Despite these opportunities, certain medical students contemptuously dissociate themselves from CAMSI, calling it "undergraduate politics". Be this true, the everyday CAMSI "politician" has consistently proven himself to be the best equipped to unravel the mysteries of interneship and practice and to protect himself in a well informed way from trends which would be adverse to his position as a student, interne and practitioner.

3. To act as the voice and representative of medical students and internes is without doubt the most important function which CAMSI serves. In these days of continual change in medical education and life, every medical student should keep abreast of these changes, and use CAMSI to spearhead his very important role in determining what medical training is to be.

An excellent example of change is current thinking about junior interneship. For the undergraduate, there is the distinct possibility that junior interneship will become a fifth medical year in which he will complete his training in a hospital

chosen from a small number approved by his medical school. As witness this trend, one has only to look at Queens University where such a trend becomes a fact in 1959. The more generalized trend toward restricted interneship as proposed by the College of Physicians and Surgeons of Ontario is evidenced by the recent passage of a ruling which states that 1961 and future graduates who wish to practise in Ontario must have completed an approved junior rotating interneship in a *Canadian* hospital approved by the Canadian Medical Association.

For those interning, or about to interne, the interneship question is one of paradox. We in Canada are privileged to have the opportunity to interne in excellent Canadian hospitals with good training programs. But while interne training is constantly improving, consider the hospitals' lack of progress in internes' remuneration, housing, and other problems. For economic reasons, junior internes, despite the fact that they are a most important part of the hospital team, are treated in an almost mediaeval manner. Remuneration is totally inadequate in most cases with the result that many graduates simply cannot afford to interne in some hospitals.

And no concessions are made toward the married interne. Many hospital administrators and medical educators feel that medical students and internes who marry during their period of training do so of their own volition—which is true. Upon this premise they avoid any responsibility to provide married quarters and adequate remuneration. This is particularly backward thinking in an age when young men and women are having to take more years of training than ever before to qualify themselves in their chosen profession.

Contrast this thinking with that of many American colleges and hospitals. There, the medical student and interne have been accepted as the natural product of a major sociological revolution which began when returning servicemen brought along their families to university and proved that marriage and knowledge did mix. Because of this attitude, the married man is no longer penalized, but is given an opportunity to maintain a decent standard of living during his training.

The entire problem of junior interneship is one which CAMSI has been working on and will continue to work on with a view to the advancement of education and interne conditions.

I have tried to set down in these few paragraphs why your local CAMSI committee feels that CAMSI is a very important part of every medical student's and interne's life. We encourage your interest and solicit your participation in all of CAMSI's activities. Your CAMSI officers stand ready to serve you in any way possible.

George J. Langmyhr, 5T8
Retiring Senior CAMSI Officer

MITRAL STENOSIS

VERA HELLER, 5T8

THIS paper will review mitral stenosis under the following headings: etiology, incidence, pathology, physiology, clinical features, treatment, and course and prognosis.

Etiology

Mitral stenosis is almost always the result of rheumatic fever. Rheumatic carditis refers to active inflammation of the heart. The sequelae, which include valve sclerosis, patchy myocardial fibrosis, and adherent pericardium, are usually described under the general heading of rheumatic heart disease. The mitral valve is involved in 85 per cent of cases of inactive rheumatic heart disease. The aortic valve is involved in 44 per cent of cases, the tricuspid in 15 per cent, and the pulmonary in 1 per cent.

The early and active stage of rheumatic endocarditis results in mitral insufficiency due to imperfect closure of the mitral orifice. Mitral stenosis develops gradually after the active rheumatic infection. The lesion takes at least two years, and usually much longer, to develop sufficiently to give rise to physical signs.

In rare instances mitral stenosis is not due to rheumatic endocarditis. It may be a congenital lesion due to anomalous development such as congenital mitral atresia. Functional mitral stenosis may result from obstruction of the valve orifice by bacterial vegetations, atrial thrombi or tumors.

Incidence

Approximately 5 per cent of healthy young adults give a previous history of rheumatic fever in childhood. It is clear, therefore, that all patients who have rheumatic fever do not later develop rheumatic heart disease. According to Wood (1956), 75 per cent of children who have their first attack of rheumatic fever before they are five years old, and 50 per cent of those whose first attack occurs after the age of ten, subsequently develop rheumatic heart disease. In Britain, approximately 1 per cent of the population between the ages of 18 and 44 has mitral stenosis.

The M : F sex ratio in pure mitral stenosis is 4 : 1; when there is trivial incompetence as well it falls to 3 : 1, and when there is serious incompetence the ratio is unity.

Pathology

Following marked or repeated inflammation from a rheumatic infection, healing results in contracting scar tissue with all grades of deformity. Two processes in particular cause the defective function:

(1) Fusion of the cusps at their edges causing both stenosis (narrowing of the ostium) and regurgitation (leaking back of the blood through the incompetent valve).

(2) Fusion of the chordae tendineae with shortening.

In chronic cases the fusion of cusps is so marked that only a small opening, often described as "buttonhole", remains where the freely acting mitral cusps should be.

In view of the pathology it is clear that mitral stenosis is almost always combined with some degree of mitral regurgitation. Stenosis usually predominates, and the associated mitral incompetence is relatively unimportant.

Physiology

The effects of mitral stenosis on the heart and lungs are due to the obstructive lesion between the left atrium and ventricle. The bodily response to this obstruction is initially twofold. There is a rise of pressure proximal to the obstruction—that is, in the left atrium, pulmonary veins, pulmonary capillaries, pulmonary artery and right ventricle. The amount of blood passing through the obstructed area—the cardiac output—becomes reduced.

The size of the orifice of the normal mitral valve in an adult is about 5 square centimeters. The pressure in the left atrium is normally about 5 millimeters of mercury. The normal cardiac output is about 5.5 to 6.0 litres per minute. Critical narrowing can be said to occur when the orifice is about 1.0 square centimeter. (This is critical in the sense that all patients are then thoroughly symptomatic.) The pressure in the left atrium at rest is then near 25 millimeters of mercury, and the cardiac output has fallen to 4.0 or 4.5 litres per minute.

Any rise of pressure in the left atrium, of course, is accompanied by a similar rise of pressure in the lungs and right ventricle. The *locus minoris resistentiae* of this circuit is the pulmonary capillary bed. Any rise of pressure above the osmotic pressure of plasma (25 millimeters of mercury) results in a transudation of fluid from capillaries to alveoli. Thus, at a valve size of 1.0 square centimeter with a pressure in the left atrium, and therefore in the pulmonary capillaries, at or about 25 millimeters of mercury, the patient becomes almost bedridden. This is because mild activity or emotion produce a rise of pressure in the pulmonary capillaries above the osmotic pressure of plasma, and there is a transudation of fluid from capillaries to alveoli with microscopic or gross pulmonary oedema. Moreover, the pulmonary vessels are so engorged and distended with blood that there is a diminished air space and vital capacity.

One of the earliest manifestations of mitral stenosis is radiologic enlargement of the left atrium, reflecting the increase in pressure within that chamber. This enlargement consists of hypertrophy and dilatation, and frequently precedes the apical diastolic murmur. Not until the valve orifice approaches 1.0 square centimeter do the pulmonary vascular markings become prominent and radiologic evidences of pulmonary oedema appear. This initial bodily response to mitral valve obstruction is not accompanied by enlargement of the pulmonary artery, of the right ventricle or of the heart as a whole. Enlargement of these structures does not occur as a result of mitral stenosis alone but only as a consequence of mitral stenosis combined with changes in the pulmonary blood vessels. The syndrome described this far is one of mitral stenosis of varying degree, culminating in a valve size of about 1.0 square centimeter. At this point respiratory distress may be devastating, but except for the left atrium and pulmonary vascular markings, the heart is of perfectly normal size.

In the majority of patients it is only at this point, when pulmonary oedema impends as a chronic state, that pulmonary vascular changes appear. The normal lung offers little resistance to blood flow and large volumes of blood pass through the pulmonary vasculature at low pressures. In severe mitral stenosis, however, the resistance offered by the pulmonary vessels increases as a result of structural changes in arterioles and small arteries. The thickened walls of capillaries and small arteries result in great difficulty in the transfer of oxygen and CO_2 from the inspired air to blood stream. Thus, two

stenoses are present in the lesser circuit —one at the mitral valve and one in the lung. The stenosis in the lung has all degrees of mildness and severity. In the most severe forms, the pulmonary vascular resistance may increase twenty times, and may offer a greater barrier to blood flow than the mitral stenosis itself.

The effect of this pulmonary vascular obstruction is again twofold: pressure proximal to it in the pulmonary artery and right ventricle rises; blood flow, or cardiac output, falls even farther—to as little as 3 litres per minute. The decline in output allows the mitral valve to become smaller, as little as 0.3 square centimeter. With the two resistances in series, pressure in the pulmonary artery, which is normally 25 millimeters of mercury systolic, 9 diastolic, may exceed the arterial pressure in the systemic circulation. Pressures as high as 140 systolic, 75 diastolic, have been recorded in the pulmonary artery. It is the right ventricle that must pump blood at this pressure into the pulmonary artery. In doing so, it becomes hypertrophied and eventually dilates and fails. It is only when pulmonary vascular disease is superimposed on the mitral stenosis that the right ventricle and pulmonary artery become enlarged—and in severe cases they may become huge. Only then does the transverse diameter of the heart become abnormal. The left ventricle and aorta do not partake in this enlargement. In fact, because the cardiac output is reduced, they become smaller than normal and appear hypoplastic. In some cases the left ventricle may appear slightly prominent due to displacement by enlarged structures on the right side of the heart.

Clinical Features

STAGE OF COMPLETE COMPENSATION

Cardiac symptoms may be completely absent in patients with physical signs of mitral stenosis. The perfectly compensated, asymptomatic patient with mitral stenosis may live a normal life span and engage in normal physical activities. But he is subject to the same complications as patients with more severe mitral lesions. Repeated rheumatic infections, progressive contraction of a scarred valve, or secondary calcification may intensify the obstruction and produce circulatory disturbances in a patient hitherto asymptomatic. Bacterial endocarditis, atrial fibrillation, embolism, pulmonary infections, and acute pulmonary oedema may suddenly abbreviate a previously uneventful course.

STAGE OF PULMONARY CONGESTION

The symptoms of mitral stenosis are almost solely due to the limited air space and the impaired exchange of carbon dioxide and oxygen in the lungs. In other words, when compensation is imperfect and there is evidence of pulmonary congestion, the classical symptoms of mitral stenosis occur. The term left atrial failure is often used when the left atrium, although dilated and hypertrophied, is no longer able to eject or accommodate the excess of blood dammed up behind the mitral obstruction. Strictly speaking, however, it should be noted that the pulmonary congestion is not due to a failure of the myocardium, but rather to the mechanical effect of the stenosed mitral valve.

The following are the chief manifestations of mitral stenosis in the stage of pulmonary congestion:

Dyspnoea is the chief symptom of mitral stenosis. It is related to the pulmonary congestion and rigidity of the lung. As a result of these changes greater strain and work are imposed on the muscles of respiration—in other words, respiration becomes laborious. Dyspnoea on effort is an early symptom. An indication of more severe pulmonary engorgement and vascular sclerosis is dyspnoea

at rest or in paroxysmal attacks when the heart rate suddenly increases.

Uncontrolled atrial fibrillation may cause dyspnoea because the rapid heart rate tends to increase the output of the right ventricle while depriving the left of sufficient diastolic time in which to fill. It should be understood that shortening diastole interferes little with ventricular filling when the atrioventricular valve is normal, but considerably when it is stenosed.

Orthopnoea occurs in the majority of patients with severe mitral stenosis. Sitting up with legs down lowers the right atrial pressure and thus diminishes the output of the right ventricle. This in turn lowers the left atrial pressure and therefore the pulmonary venous and capillary pressures. In the horizontal position these effects are reversed so that transudation of fluid from the pulmonary capillaries into the interstitial tissue is encouraged.

Cyanosis in the face and hands is the result of pulmonary congestion. A mild degree of cyanosis often produces early the so-called mitral facies. This is characterized by a cyanotic flush over the malar regions and a dusky cyanosis of the lips. The cold extremities are due to peripheral vasoconstriction secondary to a low cardiac output—and therefore are seen especially in cases with a high pulmonary vascular resistance.

Palpitation is an early symptom which occurs almost as frequently as dyspnoea. Palpitation may be due to extracardiac factors such as indigestion, excessive caffeine, alcohol or tobacco, exertion or excitement, but it appears to be induced by these causes much more readily in the heart with mitral disease than in the normal one.

Rapid irregular palpitation in cases of mitral stenosis is commonly due to paroxysmal or uncontrolled atrial fibrillation. The onset of fibrillation frequently produces palpitation, but when fibrillation is established and associated with a slow ventricular rate, many patients are unaware of its presence.

Hemoptysis occurs in approximately 10 per cent of cases of mitral stenosis, and it may occur late in the disease or it may be the initial complaint. There are several possible causes of hemoptysis. First of all, as a result of pulmonary engorgement and increased pressure in the pulmonary capillaries, a transudation of fluid from capillaries to alveoli takes place. Secondly, small congested capillaries may rupture into the lungs. The communications between the pulmonary and bronchial veins enlarge and become varicose as a result of pulmonary congestion. Rupture of these varices of the bronchial veins may be another source of bleeding. Finally, hemoptysis may be due to pulmonary embolism and infarction, particularly in patients with atrial fibrillation.

Cough is frequently present and is worse at night and after physical exertion. As a rule it is due to pulmonary congestion, but occasionally it is due to pressure of a large left atrium on the bronchial tree.

Acute pulmonary oedema is much less frequent in mitral stenosis than in aortic valvular lesions. Nevertheless, patients with severe mitral stenosis may suffer recurrent attacks of acute pulmonary oedema with dyspnoea, orthopnoea, and expectoration of frothy, blood stained sputum. The attacks are less sharply limited to the night and the horizontal position than in cardiac "asthma" due to left ventricular failure. That acute pulmonary oedema occurs so much less frequently in pulmonary congestion of mitral stenosis than in that of left ventricular failure may be due to the more gradual development of pulmonary congestion in the former and the resultant better pulmonary accommodation. Dim-

inished permeability of thick capillaries may be a factor.

Attacks of frank pulmonary oedema occur in about 10 per cent of all cases of mitral stenosis in which the mitral orifice is critically reduced. Precipitating agents include effort, emotion, pregnancy, respiratory infections, uncontrolled atrial fibrillation, and anaesthesia.

The most plausible explanation for the occurrence is the sudden intensification of pulmonary stasis in an already congested lung, owing to an increase in venous return to, and output from, the right heart. This increases the pulmonary capillary pressure which rises significantly above the colloid osmotic pressure and results in transudation of plasma fluid into the pulmonary alveoli.

Vague precordial sensations occur occasionally in mitral stenosis. Most often they are due to extracardiac or superimposed neurosis. Definite angina pectoris with typical radiations occurs occasionally and is probably due to associated aortic or coronary artery disease.

Hoarseness is uncommon. However, when present it is due to the compression of the left recurrent laryngeal nerve between the dilated left pulmonary artery and the aorta.

Dysphagia is an uncommon symptom resulting from pressure of a dilated left atrium on the oesophagus.

Weakness is a common complaint, and it may be related to the excessive work of respiration or to an inadequate cardiac output.

Arrhythmias occur frequently at this stage. Atrial fibrillation is the most characteristic and important arrhythmia. It may be paroxysmal or persistent. The cardiac output may diminish twenty to twenty-five per cent when atrial fibrillation occurs in patients with mitral stenosis. However, if the ventricular rate can be kept slow, cardiac efficiency need not be appreciably altered.

STAGE OF RIGHT-SIDED HEART FAILURE

Right heart failure is a common termination of mitral stenosis. It follows a period dominated by symptoms of pulmonary engorgement. Certain additional symptoms and signs are intrinsic in right sided heart failure, and result from engorgement of the systemic venous system. These include engorgement of the cervical and other superficial veins, enlargement of the liver, peripheral oedema, and transudates into the serous cavities.

Physical Signs in the Heart

There are five important auscultatory signs of mitral stenosis: (a) a mitral diastolic murmur, (b) a mitral presystolic murmur, (c) an accentuated first heart sound at the apex, (d) an opening snap of the mitral valve, and (e) an accentuated second sound at the pulmonary area.

(a) The characteristic sign is an apical, mid-diastolic murmur. The murmur is rough, rumbling and low-pitched. It begins after a definite period of time following the second sound. The murmur is localized at the apex in an area 2 to 3 centimeters in diameter. The bell type of stethoscope transmits it better than the diaphragm. It is best heard when the patient lies on the left side and when the velocity of circulation is increased, as after exercise.

The murmur is due to a vibration of heart walls and valve caused by a rush of blood through the stenosed mitral valve into the left ventricle. The murmur is loudest in those phases of diastole when the velocity of blood pouring into the ventricle is greatest, e.g. during those portions of diastole when the pressure difference between the left atrium and left ventricle is greatest. The murmur is loudest, then, early in diastole. As diastole proceeds and the force of the blood diminishes, the murmur tends to fall off in intensity.

(b) There is another increase in the speed of blood flow from auricle to ventricle in pre-systole due to atrial contraction. If, because of short diastole (tachycardia) or marked valvular stenosis, there is still room for more blood in the ventricle, the increase in the flow of blood through the stenosed mitral valve will accentuate the diastolic murmur just before the first sound, or make it audible again after it has disappeared entirely. Occasionally it is present without a mid-diastolic murmur. It is not present in atrial fibrillation in which condition there is no effective atrial contraction.

(c) The first heart sound is accentuated in practically all cases of pure mitral stenosis, provided the valve is not heavily calcified. The first heart sound is due to mitral (and tricuspid) valve closure. Its intensity depends chiefly upon the position of the cusps at the beginning of ventricular systole. The loudest first sound is produced when atrial contraction forces the leaflets wide open immediately before the ventricles contract (short PR interval, around 0.1 second), but when there is a relatively long delay between atrial and ventricular excitations (long PR interval, around 0.2 second), the cusps may float into apposition before the ventricles contract and hence shut quietly. In mitral stenosis, the pre-systolic atrial contraction forces the mitral cusps to remain open until the last possible moment, so that when the left ventricle contracts, they slam together.

(d) The opening snap is a sharp, high pitched sound made by the resistant cusps of the mitral valve when they are flung forward into the cavity of the left ventricle at the beginning of ventricular filling. The snap occurs 0.08–0.10 second after aortic valve closure, and is best heard down the left sternal border just superior and medial to the nipple line and at the mitral area. The opening snap occurs slightly before the instant at which a third heart sound would be heard, and can be distinguished from a third heart sound by its relatively high pitch. The opening snap is heard in practically all cases of pure mitral stenosis of more than trivial degree, provided the valve is not heavily calcified and rigid.

(e) The second sound in the pulmonary area is usually intensified in mitral stenosis. This is due partly to the rise in pressure in the pulmonary artery, and partly to the rotation of the pulmonary artery and conus which brings them closer to the chest wall.

Treatment

The management of mitral stenosis is both medical and surgical.

MEDICAL

The physician's responsibilities include guiding the patient's general living habits as well as treating the various complications that may occur. In the inactive or symptom-free stage, the patient is advised to avoid extreme fatigue, unnecessary exposure to wet and cold, and exposure to individuals with active or recent respiratory infections. He is advised on occupational problems and given optimistic encouragement.

As the disease progresses, the physician is required to prevent and stop paroxysmal dyspnoea and acute pulmonary oedema, control the cardiac rhythm, control heart failure, steer a woman through or away from pregnancy, select cases for valvotomy, and deal with any other complication that may arise.

SURGICAL

Mitral valvotomy was introduced by Harken (1948) and Bailey (1949) in the United States, and by Brock (1950) in England. Since then thousands of cases of mitral stenosis have been relieved

surgically. The easiest and best approach is through the left atrial appendage. In the simplest cases the fused commissures are separated digitally, and the split is continued as far as the ring on both sides.

In general, any patient who is *suffering* from the effects of mitral stenosis requires valvotomy, and any patient who is able to continue his normal occupation without distress does not. There are several reasons for not operating prematurely: (1) The surgical mortality in relatively mild, uncomplicated cases is not negligible (1.7 per cent in one series); (2) the risk of cerebral embolism at operation is not confined to advanced cases; (3) a technically good result is only achieved in 75 per cent of cases, and is no more likely when the stricture is relatively mild than when it is extreme; (4) post-operative re-stenosis does occur. Mitral valvotomy is contraindicated in the presence of mitral insufficiency.

The chief dangers of deferring operation are cerebral embolism and acute pulmonary oedema, both of which may occur unexpectedly in relatively mild cases.

Course and Prognosis

The initial rheumatic attack usually occurs between the ages of 8 and 12 years. The worst cases die within 5 years, the mortality in the active phase being 6.5 per cent. The vast majority of those that recover become temporarily free from symptoms.

The symptom-free period lasts for an average of 20 years. Around the age of 30 true effort dyspnoea develops, and usually increases a grade every 2 to 3 years, so that total incapacity is reached in 7 to 8 years. The average duration of total incapacity is about 3 years, so that the total period of symptoms occupies about 10 years, and the average age of death is about 40.

There is, of course, a very wide variation in behaviour from case to case; some patients die in adolescence and many individuals live a practical, normal life span, and engage in normal activities.

The presence of persistent rheumatic activity, a large heart, persistent atrial fibrillation, heart failure and embolism all make the prognosis unfavourable.

Favourable factors in prognosis are: absence of rheumatic activity, survival beyond adolescence, absence of symptoms and signs of heart failure, little or no cardiac enlargement, and a favourable economic and social status which permits the avoidance of undue physical and mental stress, and climatic hazards.

Acknowledgement

The author is very grateful to Drs. W. E. Hall and D. B. Moran for their interest and helpful suggestions in the preparation of this paper.

Bibliography

1. Dexter, L., *New Eng. Jour. of Med.*, **254**: No. 18, 1956.
2. Friedberg, C. K., Diseases of the Heart, 1956.
3. Wood, P., Diseases of the Heart and Circulation, 1956.
4. White, P., Heart Disease, 1950.
5. Harrison, T. R., Principles of Internal Medicine, 1954.
6. Rushmer, R., Diagnosis of Cardiac Disease, 1955.

CONGENITAL HEART DISEASE

H. KLEIMAN, 5T8

Definition

CONGENITAL heart disease refers to those conditions in which anatomical defects in the structure of the heart and great vessels exist due to faulty or arrested development during their formative period.

Classification

1. Derivatives of the Aortic Arches
   - i. Vascular rings:
     - (a) double aortic arch
     - (b) others
   - ii. Coarctation of the aorta
   - iii. Patent ductus arteriosus
2. Cardiac Septa and Atrio-ventricular Valves
   - A. Atrial Septal Defects
     - i. Patent foramen ovale
     - ii. Foramen secundum defect
     - iii. Foramen primum defect
     - iv. Lutembacher's syndrome
   - B. Ventricular Septal Defects
     - i. Small defect (Maladie de Roger)–usually low in septum
     - ii. Large defects—usually high in septum
     - iii. Large defects and increased pulmonary resistance (Eisenmenger's syndrome)
     - iv. Single ventricle
       - (a) pulmonary artery from main chamber
       - (b) pulmonary artery from rudimentary chamber
   - C. Atrio-ventricular Valves
     - i. Tricuspid atresia
     - ii. Ebstein's disease
     - iii. Atrioventricularis communis
3. Truncus Arteriosus Partitioning and Semilunar Valves
   - i. Persistent truncus arteriosus
   - ii. Aorta-pulmonary septal defect
   - iii. Transposition of the great vessels
   - iv. Pulmonary stenosis—pure
     - (a) infundibular
     - (b) valvular
   - v. Tetralogy of Fallot
   - vi. Pulmonary atresia (Pseudotruncus arteriosus)
   - vii. Aortic stenosis
     - (a) subvalvular
     - (b) valvular
4. Others
   - i. Subendocardial fibroelastosis
   - ii. Anomalous pulmonary venous drainage
     - (a) complete
     - (b) partial
   - iii. Dextrocardia
     - (a) with situs inversus
     - (b) without situs inversus

1. Derivatives of the Aortic Arches

Embryology

In vertebrate embryos six pairs of aortic arches are formed connecting the ventral and dorsal aortas on each side. The early degeneration of the first two aortic arches and the fact that the 5th never appears in mammalian embryos, except as a vestigial vessel, leaves only the ventral and dorsal aortic roots and the 3rd, 4th and 6th aortic arches to play an important role in the formation of adult vessels.

The 3rd aortic arches form the proximal portion of the internal carotid arteries.

The 4th aortic arch on the left forms the arch of the adult aorta. On the right it forms the proximal part of the subclavian artery. The innominate artery is formed by the short sections of the right ventral aortic root between the 4th and 6th arches.

The 6th aortic arches give off branches to the lungs. The right side of the 6th aortic arch loses communication with the dorsal aorta. On the left, however, communication is retained with the dorsal aortic root and the part of the 6th arch between the origin of the left pulmonary trunk and the dorsal aorta is called the ductus arteriosus.

Of great importance in the development of clinically important arch anomalies is the fact that the heart and great vessels are carried caudad in the body during their development. This means that certain vessels such as the subclavian arteries, which are firmly anchored to the body wall distally, shift their point of origin from the dorsal aortic roots to a higher and higher position as the heart moves caudad in the body until they arise from the aortic arch. Thus, the more cephalic segments of the dorsal aortic roots are relatively shortened as the heart moves caudad. The significance of these changes is that relationships between the vessels and associated structures such as the esophagus and trachea are greatly altered during this period, and vascular abnormalities are therefore apt to produce symptoms by interference with the related structures.

i. VASCULAR RINGS

These are congenital anomalies of the aortic arch and its tributaries causing varying degrees of compression of the trachea and esophagus. There is no cardiac dysfunction. There are five such anomalies of which the three most important are double aortic arch, right aortic arch with left ligamentum arteriosum, and anomalous right subclavian artery.

(a) *Double Aortic Arch*

When both the right and left 4th arches and dorsal aortic roots persist, there results an aortic ring. Due to the shortening of the upper aortic segments as previously mentioned, this ring tends to be pulled closely about the trachea and esophagus so that it interferes with swallowing. The usual case is that one of the aortic arches is definitely smaller than the other.

ii. COARCTATION OF THE AORTA

In the past coarctation was regarded as having two distinct forms, i.e. infantile and adult. Since this arbitrary classification was made in 1903 it has been seen that a great deal of overlapping exists. It seems best to classify coarctations as to their site and nature since this bears on the surgical treatment. Most coarctations occur near the site of the ligamentum arteriosum and are either abrupt or elongated in nature.

The embryology of this condition is not clear, and many theories have been advanced. One is that there is a tendency for the aorta to be constricted near the site of the ductus arteriosus when this structure closes after birth. Another states that the isthmus, a slightly narrowed area between the left subclavian artery and ductus arteriosus part of the aorta, fails to enlarge after birth. Normally there is an increased flow in the upper aorta after birth when the ductus closes since the total systemic blood flow is expelled from the left ventricle for the first time. This increased flow is said to cause the isthmus to become fully dilated at four months.

It would seem that both these theories are dependent on a sufficient upper aorta flow to keep the aorta opposite the ductus from constricting when the ductus closes and to widen the isthmus and prevent exaggeration of its narrowing. It is not surprising, therefore, that in many cases anomalies are associated with decreased flow or pressure in the upper aorta. These are subendocardial fibrosis, aortic valve abnormalities and patent ductus arteriosus.

The problem of a block in the aorta

is met by (1) increased pressure in the aorta proximal to the coarctation, (2) vasoconstriction of the arterioles to maintain a high diastolic pressure, and (3) opening up of collateral circulation to by-pass the coarctation. Of course, the left ventricle work is increased due to the coarctation, and left ventricular failure is a complication. The high pressure in the vessels of the upper half of the body is also the cause of cerebrovascular accidents.

iii. PATENT DUCTUS ARTERIOSUS

The purpose of the ductus arteriosus in fetal life is to shunt part of the right ventricular output into the aorta and thereby avoid the pulmonary circulation which is as yet not ready to accept a larger blood volume. Following birth there is a contraction of the circularly disposed smooth muscle in its wall which reduces the flow within it. This, plus the fact that the lungs have assumed respiratory activity, aids in raising the pulmonary circulation to its full functional level. Ultimate obliteration of the lumen by overgrowth of the intimal connective tissue occurs normally in six to eight weeks.

There is no embryological explanation for failure of the ductus to obliterate. It is the most common congenital heart lesion resulting from maternal rubella.

After birth the gradual increase in the aortic pressure in response to the greater peripheral resistance in the systemic circulation will force blood into the pulmonary artery and cause pulmonary engorgement. Since oxygenated blood must be recirculated in the lungs and left heart, there is left ventricular overwork.

Occasionally in cases with pulmonary hypertension there is a shunting of unoxygenated blood from the pulmonary artery into the aorta. Right ventricular overwork is the case here.

2. CARDIAC SEPTA AND ATRIO-VENTRICULAR VALVES

A. ATRIAL SEPTAL DEFECTS

i. *Patent Foramen Ovale*

Since in an otherwise normal heart this condition is of no consequence and since it occurs frequently (20–25 per cent of post mortems) it is best to think of this condition as merely a variation from normal and not as a defect.

Shortly after birth the left atrial pressure rises and the flap is pushed tightly against the septum secundum closing the foramen ovale functionally. This abandonment of the right to left shunt plus a great deal of connective tissue proliferation of the valvula causes it to become adherent to the part of the septum secundum above the foramen ovale and thus permanently closed. This closure occurs not before the eighth month postnatally and frequently much later.

In 20 per cent of adults a probe may be passed at post mortem from the right atrium behind the valvula into the left atrium. This is known as a patent foramen ovale. Only when the resistance to blood flow on the right side of the heart is greater than that on the left does flow through it occur since the one-way flap covering the foramen can only allow right to left flow.

ii. *Foramen Secundum Defect*

Defects at this site are due to either excess reabsorption of the septum primum so that it becomes too short to cover the foramen ovale or to an abnormally large foramen ovale so that the septum primum flap is inadequate to cover it.

iii. *Foramen Primum Defect*

These lower defects in the atrial septum are due to persistence of the ostium primum resulting from a failure of the septum primum to grow down and

reach the A-V canal cushions. Occasionally the A-V canal cushions are involved and one sees defects in the A-V valves as well.

iv. *Lutembacher's Syndrome*

This refers to an atrial septal defect with mitral stenosis, either congenital or acquired.

The effect on the circulation of atrial septal defects is a left to right shunt of oxygenated blood through the defect with resultant right heart overwork and pulmonary congestion. The left ventricle work is decreased as it receives less than the normal amount of blood. Lutembacher's syndrome, because of the increased left atrial pressure secondary to the mitral stenosis, causes the left to right shunt to be greater than it otherwise would be.

B. VENTRICULAR SEPTAL DEFECTS

Defects are usually seen in the upper membranous part. This is to be expected since it is formed from three different structures. Occasionally defects in the lower muscular portion of the interventricular septum are present.

i. *Maladie de Roger*

Roger's disease refers to a small ventricular septal defect not complicated by significant right ventricular overwork.

ii. *Large Ventricular Septal Defect*

Usually the site of the defect is in the upper membranous part of the septum.

The circulatory effects are a left to right shunt due to the pressure gradient between the left and right ventricle with resultant right heart overwork and pulmonary congestion. However, in contradistinction to an atrial septal defect the left ventricle work is increased.

iii. *Eisenmenger's Syndrome*

The pathological findings of this condition are the same as those of Tetralogy of Fallot except that there is no pulmonary stenosis. The cyanosis is not due merely to an over-riding aorta receiving blood from the right ventricle, but is due to a right to left interventricular shunt. The explanation of the right to left shunt without pulmonary stenosis is on the basis of the presence of pulmonary hypertension or pulmonary vascular obstruction (Wood 1956). It would seem that the over-riding of the aorta is not physiologically relevant. Thus, Eisenmenger's disease should be in reality called "pulmonary hypertension with a reversed inter-ventricular shunt". The cause of the high pulmonary resistance is not known, but it is thought by some to represent a persistence of the fetal type of pulmonary circulation in which a high resistance is maintained by thick muscular arteries, the object being to divert the blood flow away from the lungs to the descending aorta via the ductus arteriosus.

iv. *Single Ventricle* (*Cor Triloculare*)

Since there are usually two chambers present, a rudimentary and a main one, this condition cannot be regarded anatomically as the extreme example of a ventricular septal defect. Because the rudimentary chamber is the remainder of the bulbus cordis, it would be expected that the pulmonary artery would originate from it, but the aorta usually does, thus constituting transposition of the vessels as well. The pulmonary blood flow depends on the chamber from which the pulmonary artery originates. If it is from the main chamber, most of the blood in the heart is circulating through the lungs and cyanosis is minimal in spite of mixing of the right and left atrial blood in the common ventricle. If the pulmonary artery originates from the rudimentary chamber, then most of the blood in the heart is not circulating through the lungs and cyanosis is evident.

C. ATRIO-VENTRICULAR VALVES

i. *Tricuspid Atresia*

This lesion is likely the result of improper division of the atrioventricular canal by the ventricular septum growing up from below. The blood exits from the left atrium via a patent foramen ovale or an atrial septal defect, and mixes with the oxygenated blood in the left atrium. If there is a ventricular septal defect, the blood reaches the pulmonary circulation via the right ventricle. If there is none, then a patent ductus carries blood to the pulmonary circulation from the aorta. Transposition of the pulmonary artery and aorta is often associated with this condition, and in these cases blood reaches the right ventricle from the left ventricle via a ventricular septal defect, and then passes into the transposed aorta.

ii. *Ebstein's Anomaly*

In this condition the posterior and frequently the septal cusps of the tricuspid valve are attached to the ventricular wall below the usual site of attachment which is the annulus fibrosis. Thus, the upper part of the right ventricle is incorporated into the cavity of the right atrium. As a result the right atrium is greatly enlarged and the right ventricle is small. The tricuspid valve is usually functional, but may show regurgitation. The association of an atrial septal defect or a patent foramen ovale accounts for the mild cyanosis, there being a variable right to left atrial shunt.

iii. *Atrioventricularis Communis*

Here there is a common A-V canal due to failure in development of the canal cushions. This condition is, therefore, associated with defects in the upper part of the ventricular and the lower part of the atrial septa. The effects are similar to those of a very large ventricular septal defect.

3. TRUNCUS ARTERIOSUS PARTITIONING AND SEMILUNAR VALVES

Embryology

The partitioning of the truncus arteriosus begins distally between the roots of the 4th and the 6th aortic arches, and progresses spirally back through the truncus toward the ventricles. The division is effected by the growth of a pair of ridges from the inside wall of the truncus which cut more and more deeply into its lumen and finally meet to form a complete partition. This partition is called the aortic septum, and separates an aortic channel leading into the 4th aortic arches and a pulmonary channel leading into the 6th aortic arches. The fact that these truncus ridges pursue a spiral course as they grow toward the ventricle accounts for the way the ascending aorta and the main pulmonary trunk twist around each other as they emerge from the ventricles. Thus, the aorta comes to be in position to receive blood from the left ventricle and the pulmonary artery from the right ventricle, the division of the common ventricle into right and left parts having occurred simultaneously.

The aortic and pulmonary valves develop at a level which may be regarded as the line of demarcation between the truncus arteriosus and the tapering ventricular outlet called the conus. In the walls of both the aorta and pulmonary trunk at this level three small pads of plastic young connective tissue develop and bulge into the lumen. These gradually become moulded into the cusps of the semilunar valves.

i. *Persistent Truncus Arteriosus*

If the truncus ridges fail to develop, a persistent truncus results. Since these ridges normally grow downward into the conus and contribute to the formation of the upper part of the interventricular septum, then their absence is responsible

for a high ventricular septal defect as well as a persistent truncus.

This single arterial trunk over-rides the ventricular septum, and receives blood from both ventricles. If the truncus gives off normal sized pulmonary arteries, then there is a fairly well oxygenated mixture of blood in the truncus. Otherwise, if the pulmonary circulation is lacking, then the truncus blood is not much more oxygenated than venous blood. The two ventricles have equal pressures, but right ventricular hypertrophy is seen.

ii. *Aorto-Pulmonary Septal Defect*

Rather than absence of the aortic septum there is incomplete development of it. The defect is located just above the aortic valve.

The physiological effects are identical to those of a patent ductus. There is a shunt of oxygenated blood from the aorta to the pulmonary artery. This causes pulmonary engorgement and left ventricular overwork.

iii. *Transposition of the Great Vessels*

In this condition the ascending aorta arises from the right ventricle instead of the left and the pulmonary trunk arises from the left ventricle. The cause is a failure of the ridges of the truncus and conus to follow their normal spiral course as they develop. This malposition of the conus ridges means that they will not meet normally with the other structures which contribute to the closing of the interventricular foramen. Thus, there is usually an associated high ventricular septal defect, and this is the means by which oxygenated blood reaches the right ventricle and aorta from the left ventricle.

Since transposition alone would result in two completely separate circulations, the right ventricle pumping and receiving systemic blood and the left ventricle pumping and receiving pulmonary blood, it is obvious that shunts are necessary for survival. As well as ventricular septal defects one frequently sees an atrial septal defect, patent foramen ovale or a patent ductus arteriosus.

iv. *Pure Pulmonary Stenosis*

This may be either valvular or infundibular. The infundibular type represents a failure of expansion of the bulbus cordis to form the right ventricle so that there is obstruction at a subvalvular level. In valvular stenosis the cusps are fused into a membrane with a hole in the middle which varies in size. This type has been considered, without proof, to be the result of superimposed disease in utero on normally developed valves.

The result of the lesion is decreased pulmonary blood flow. Right ventricular work is greatly increased and failure may ensue. The opening up of a foramen ovale may occur so as to relieve the right heart pressure.

v. *Tetralogy of Fallot*

This condition may be explained embryologically as a misplacement of the spiral ridges of the truncus resulting in pulmonary stenosis and an over-riding aorta. The failure of the malplaced ridges to join the interventricular septum results in a ventricular septal defect. The right ventricular hypertrophy results secondary to the pulmonary stenosis.

The increased right heart pressure causes the ventricular shunt to be from right to left and cyanosis results. The decreased pulmonary flow is reflected in exertional dyspnoea which is marked. The right ventricular pressure is limited by the trans-septal flow in contrast to pure pulmonary stenosis, and right heart failure is thus not common here.

vi. *Pulmonary Atresia*

This condition anatomically and embryologically is an extreme degree of Fallot's Tetralogy, and should be considered as such rather than as a variant

of truncus arteriosus. In the latter there is usually no lack of pulmonary blood flow whereas in this condition as in the tetralogy this is the chief problem. Life depends on the presence of a large broncho-pulmonary anastomosis or a patent ductus anteriosus, and is usually short in duration.

vii. *Aortic Stenosis*

The anatomical types and embryological background are the same as in pure pulmonary stenosis. Whereas in pulmonary stenosis the burden fell on the right ventricle, in this condition the left ventricle bears the load. Coronary artery filling may also be interfered with, and thus the problem may be worse.

4. Other Anomalies

i. *Subendocardial Fibroelastosis*

Pathologically one sees a white thickening of the endocardium most frequently in the left heart. The underlying myocardium is thickened. The fibroelastic layer hampers blood flow within the myocardium with resultant poor muscle oxygenation and ultimate failure.

Various etiological theories such as inflammation and anoxia have been advanced but not proven.

ii. *Anomalous Pulmonary Venous Drainage*

In this condition some or all of the pulmonary veins drain into the right atrium. When the condition is complete, the right side of the heart and lungs are called on to handle a very greatly increased blood flow. The left side of the heart receives mixed blood through a patent foramen ovale or an atrial septal defect. The amount of blood which the left heart receives is decreased, and therefore it is hypoplastic.

When the anomalous drainage is only partial, the effect is exactly the same as an atrial septal defect with the usual left to right shunt.

iii. *Dextrocardia*

This condition refers to a heart in the right side of the thorax with the apex pointing toward the right. Dextrocardia with or without situs inversus (transposition of the abdominal viscera) is likely to be associated with structural cardiac lesions, especially septal defects, and this is the reason for its importance.

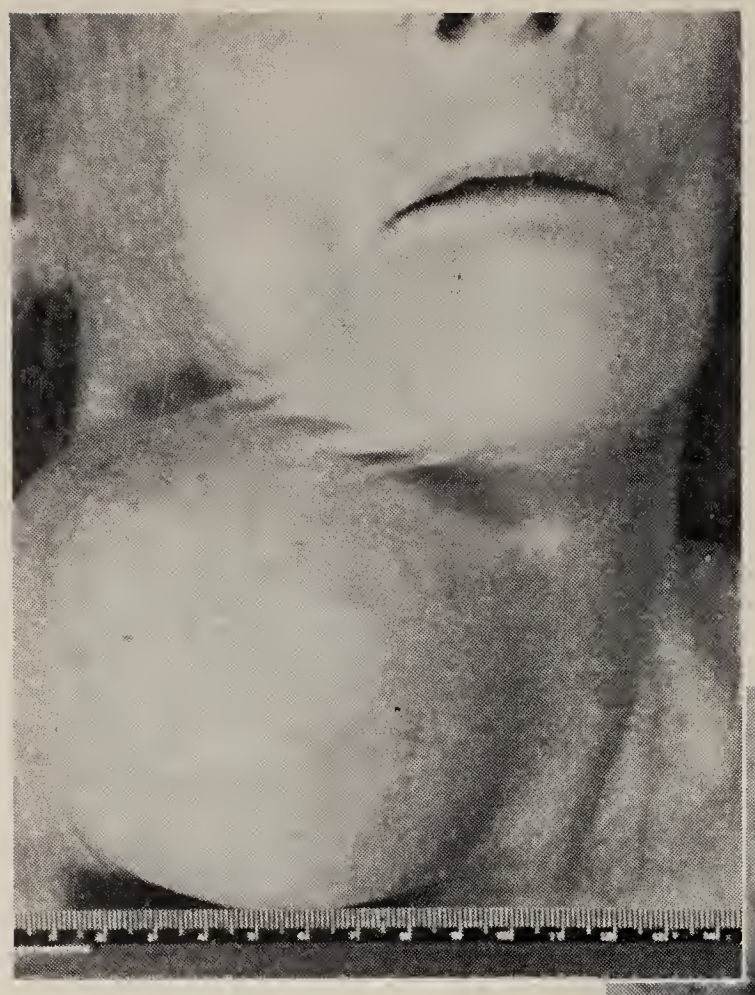
Bibliography

1. Hamilton, Boyd and Mossman: Human Embryology, 1952.
2. Patten: Human Embryology, 1953.
3. Bremer: Congenital Anomalies of Viscera, 1957.
4. Brown: Congenital Heart Disease, 1950.
5. Taussig: Congenital Malformations of the Heart.
6. White: Heart Disease, 1951.
7. Wood: Diseases of the Heart and Circulation, 1956.
8. Gross: Surgery of Infancy and Childhood, 1953.
9. Edwards: Atlas of Congenital Anomalies of the Heart, 1954.
10. Kaplan and Robinson: Congenital Heart Disease, 1954.
11. Nadas: Pediatric Cardiology, 1957.
12. Cecil and Loeb: Text of Medicine, 1955.
13. Nelson: Text of Pediatrics, 1954.
14. Patterson and McCreary: Pediatrics, 1956.
15. Friedberg: Diseases of the Heart, 1955.
16. Mechanism of Congenital Malformations, 1954, 2nd Scientific Conference, Association for Crippled Children.
17. Congenital Heart Disease, Report of the 14th M and K Pediatric Research Conference 1956.

On Inspection:

Careful observation often makes a diagnosis without the physician laying a hand or an instrument upon his patient. Here are six photographs to test your powers of observation. Each has enough clues for you to make the diagnosis.

You will find the answers on page 123.



↑

FIGURE 1. You can't miss this! Identify the lesion. Classify lumps in the neck.

→

FIGURE 2. The tape offers the key to the diagnosis of this acutely tender lesion. Give a differential diagnosis of lumps in the scrotum.

FIGURE 3. Name the apparatus, its use and advantages.

↓

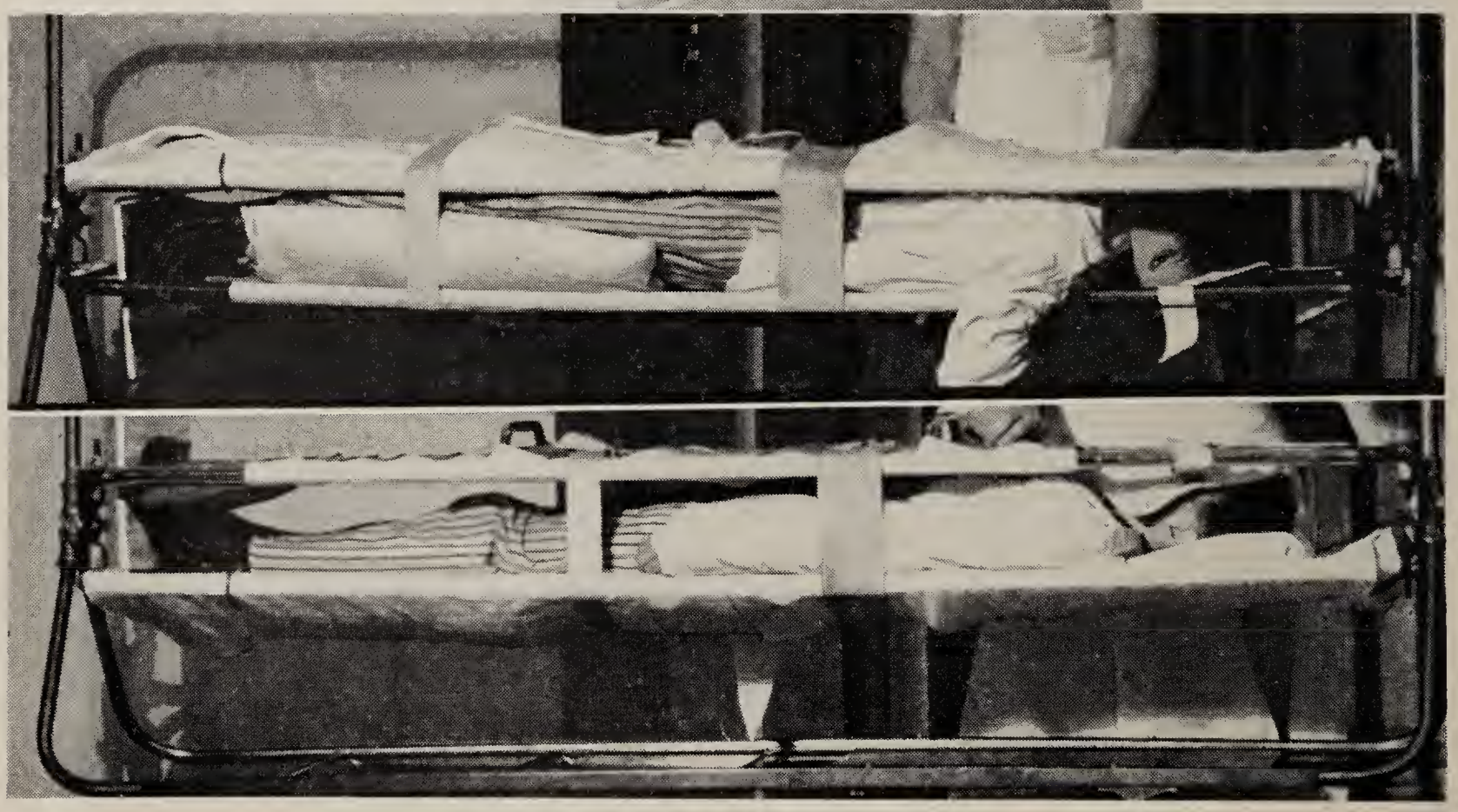


FIGURE 4. Name the apparatus and as many parts as you can. What is the basic principle behind its use?

AORTIC INSUFFICIENCY

DORIS E. KERR, 5T8

AORTIC insufficiency is an abnormal condition of the aortic valve or ring resulting in improper closure of the valve, and leading to regurgitation of blood from the aorta to the left ventricle during diastole. It is three times as frequent in males as in females.

Etiology

The most common causes are:

1. Rheumatic heart disease.
2. Syphilitic heart disease.
3. Arteriosclerotic valvular disease (Calcific aortic valvular disease).

Less common causes are:

4. Bacterial endocarditis.
5. Stretching of the aortic ring.
   (a) Chronic hypertension.
   (b) Severe anemia.
6. Trauma.
7. Dissecting aortic aneurysm.
8. Congenital defect (Biscupid aortic valve).

Pathology

1. rheumatic heart disease

Aortic insufficiency in patients below the age of 35 is almost always rheumatic in origin. The basic lesion is an inflammatory process of the valve proper. In the acute stage of rheumatic fever, tiny translucent nodules (verrucae) measuring 1 to 3 mm. in size form along the lines of closure on the surface of the valve. Later, these nodules appear more opaque, reddish gray or tawny in colour, and may become fused for a considerable distance to form a pyramidal ridge along the line of closure. Also, the nodules may form conglomerate mounds on the corpora Arantii of the valve, and there extend in rows along the semilunar cusps. Frequently a diffuse thickening of the cusps is noted. Microscopically, a non-specific inflammatory process consisting of oedema, increased numbers of capillaries, and a variety of inflammatory cells is observed in the proximal layers of the valve. Aschoff cells arranged in nodules or rows and surrounding foci of intensely eosinophilic fragmented collagen are often present.

With recurrent valvulitis the aortic cusps reveal, in addition to thickening, considerable shortening resulting from a rolling and inversion of the free margins of the cusp toward the sinus pocket. The cusps may also present adhesions at the commissures and verrucae in various stages of activity. Microscopically there is fibrosis, elastic tissue proliferation, and numerous arteries with thick muscular walls in the ring and leaflets.

Chronic valvulitis results in thickening and fibrosis with resultant loss of elasticity and narrowing of the orifice. There is deposition of calcium salts in the commissures and the cusps themselves, hyalinization of the annulus, and vascularization of the superficial layers of the valves by capillaries and thick walled vessels. Thus, the valves become insufficient due to (i) shortening, deformity and rigidity of the cusps preventing proper coaptation, and (ii) loss of tensile strength of the annulus with resultant dilatation.

2. syphilitic heart disease.

The pathognomonic change is a widening of the commissures, leading to interference with the closure of the valve during diastole. Commonly triangular hyaline plaques are present in the region of the commissures. There is a dilatation of the aortic ring caused by destruction

of the elastic tissue, and the central portions of the free margins of the cusps show thickening, eversion, rolling, and sometimes retraction resulting in an inability to occlude the aortic orifice. Microscopically, the intima of the sinus of Valsalva and the corresponding lateral portions of the cusps show degenerative, then inflammatory changes. Also, newly formed blood vessels extend through the intima to the commissures and from the base of the cusps to their lateral and proximal borders. Later, hyalinization in the region of the commissures and central portions of the cusps is observed. Hence, syphilitic insufficiency results from (i) widening of the commissures, (ii) shortening of the cusps with failure to occlude the valve orifice, and (iii) dilatation of the ring secondary to dilatation of the aorta.

3. ARTERIOSCLEROTIC VALVE DISEASE

Friedberg states that clinical evidence of aortic insufficiency has been observed in patients with marked arteriosclerotic dilatation of the aorta and hypertension, where normal aortic valves were found on postmortem examination.

Stretching of the aortic ring leads to a relative insufficiency of the aortic valve. With hypertrophy of the left ventricle, the ring is passively stretched with resultant improper closure of the cusps.

4. BACTERIAL ENDOCARDITIS

A proliferative lesion in the form of a friable vegetation forms along the line of contact of a normal or previously injured valve. The vegetations may cover the valve, and spread onto the mural endocardium. Microscopically the vegetations consist of masses of fused platelets and fibrin, with large numbers of bacteria on the surface, and an infiltration of mononuclear cells at the attachment of the vegetations to the cusp.

5. TRAUMATIC AORTIC INSUFFICIENCY

Injury may result from unusually strenuous muscular effort, or from direct trauma caused by a blow to the chest wall or a fall from a height. Examination reveals a linear tear involving one or more valve cusps and not infrequently the root of the aorta. The ruptured valve is generally diseased, but occasionally it appears to have been normal.

6. DISSECTING AORTIC ANEURYSM

Occasionally the dissection may involve the root of the aorta, causing an interference with the closure of the aortic cusps.

PATHOGENESIS

With a failure of the aortic valve to close properly, blood regurgitates into the left ventricle during ventricular diastole. The amount of the reflux depends on the size of the leak, the pressure gradient between the aorta and left ventricle during diastole, and the duration of diastole, and may amount to as much as 50 per cent of the preceding systolic discharge. The regurgitant fluid added to the volume of blood entering the ventricle from the atrium causes a greater initial ventricular volume and tension, a stronger ventricular systole, and a larger systolic discharge. With a regurgitation of 50 per cent of the ejected blood, the stroke volume must be twice the normal to maintain a normal rate of circulation through the body. A normal cardiac output is maintained by prolongation of the period of systolic ejection (the phase of isometric contraction being shortened to the same degree) as well as a more forceful contraction of the left ventricle. With increased ventricular volume and tension there is a greater ejection force, and the lower diastolic pressure in the aorta allows the heart to produce a more rapid, earlier, and more complete ejection of blood into the aorta and a sharper rise in aortic

pressure. Since more blood is ejected during the early part of systole than is normal, the pressure in the aorta and ventricle begin to drop rather rapidly during the latter part of ventricular systole. The regurgitation of blood into the ventricle together with a normal flow of blood into the capillaries causes a greater drop in pressure in the aorta during diastole and, therefore, a lower diastolic pressure.

The increased diastolic volume and intraventricular tension lead to an initial dilatation followed by hypertrophy of the left ventricular myocardium in an attempt to compensate for the load. The weight of the heart generally exceeds 500 Gm., may reach 750 or 1,000 Gm., and the hypertrophied heart is suitably named "cor bovinum". The enlargement involves chiefly the outflow tract in the early stages, that is, the anterior half of the left ventricle and interventricular septum, and the endocardium of the region is often whitened and thickened, with crescentic pockets below the aortic valve.

Clinical Features

In the absence of complications, patients with pure or predominant aortic insufficiency may occasionally live a normal life span without knowledge of their disease or without any significant symptomatology. Occasionally there are subjective disturbances even with adequate compensation. The forceful heave of the enlarged heart may be very discomforting, particularly on lying down. There may be dizziness on sudden change of position due to a transient cerebral anaemia from rapid changes of pressure in the cerebral vessels.

Angina is rarely due to an uncomplicated lesion. In lues, it originates from a luetic narrowing of the coronary ostia. In rheumatic aortic insufficiency, it has been attributed to (1) decreased coronary flow due to the low diastolic pressure, and (2) an increased demand for blood resulting in increased work of the hypertrophied heart.

Left ventricular failure may occur after a period of nearly adequate compensation, its earliest symptom being progressive dyspnoea on exertion. Paroxysmal dyspnoea is characteristic, appears in sudden attacks lasting up to fifteen minutes, and may arise after exertion or during sleep. It is especially frequent in luetic disease.

Ultimately there is dilatation of the right ventricle, tricuspid insufficiency, and right atrial enlargement. With a rise in venous pressure in the venae cavae and peripheral venous system, the typical manifestations of right sided failure are noted—engorgement of the neck veins, peripheral oedema, and enlargement of the liver.

CARDIAC SIGNS

A heaving apex impulse is noted to the left of and below its usual site, with occasional diffuse systolic depression of the chest wall medial to the apex impulse. Percussion reveals cardiac enlargement. On auscultation a soft blowing high pitched diastolic murmur is heard best in the third or fourth interspace along the left border of the sternum, starting immediately after the second sound. The murmur may be transmitted to the apex and left axilla, and is best heard with a Bowles type of stethoscope chest piece when the patient is in an upright position and leaning forward. The murmur usually continues through all or most of diastole showing a gradual decrease in intensity, and occasionally masking the second sound. In lues, the murmur is often louder and lower pitched than in rheumatic heart disease, while with a traumatic etiology it is often extremely loud and musical in quality (seagull murmur).

Occasionally a low rumbling late diastolic or presystolic apical murmur is

heard, indistinguishable from the characteristic murmur of mitral stenosis. This is the Austin Flint murmur, and is generally heard when left ventricular failure is present. Gould suggests that eddy currents are set up in the stream of blood passing from the left atrium to the ventricle during ventricular diastole, possibly because of partial closure of the aortic cusp of the mitral valve by the regurgitating aortic stream, and also because of enlargement of the left ventricle.

PERIPHERAL SIGNS

The high systolic pressure and low diastolic pressure produce a sharply rising wave front which is transmitted to the periphery as a water hammer pulse, giving rise to a tap felt by the palpating fingers and to the pistol shot pulse heard over the arteries in the inguinal canal. Diastolic pressure may be 60 mm. of mercury or lower—often sounds continue to be heard until pressure in the cuff is zero. Pulse pressure is high, usually exceeding 60 mm. of mercury. The wide oscillation in pressure in the aorta causes sufficient fluctuation in the flow of blood into the capillaries to produce a rhythmic variation in the colour of the nailbed, designated the capillary or Quincke pulse. This is demonstrated by light compression of the finger nail, transillumination of the finger tip, or pressure of a glass slide against the lips, and may occur in any condition where there is sufficient arteriolar relaxation to allow direct transmission of the arterial pulse wave to the capillaries. Arterial pulsations may be visible in the neck vessels due to a sudden filling of large collapsed arteries. Ophthalmoscopic examination may reveal pulsations of the retinal arteries as well as veins. The slight physiological excess of blood pressure in the femoral artery over that in the brachial artery is greatly exaggerated in aortic insufficiency—the difference approaching 60 to 100 mm. of mercury.

Normally a systolic murmur is heard over the femoral arteries with slight compression of these vessels. In aortic insufficiency, a diastolic murmur is also audible above the compressed vessel, and this is called Duroziez's sign. It has been attributed to retrograde flow during diastole, and may occur in any condition causing a large primary pulse wave, a steep predicrotic notch, and a conspicuous dicrotic wave. Compression of the vessel halts the blood flow at the predicrotic notch, and is overcome by the dicrotic wave. Thus, above the obstacle, the dicrotic wave is exaggerated, and a diastolic murmur is heard.

X-ray reveals enlargement of the left ventricle and prominence of the aorta. The aortic knob is accentuated by the unfolding of the arch which causes the superior vena cava to be pushed to the right. Fluoroscopy reveals exaggerated pulsations of the left ventricle and aorta.

Course and Prognosis

The average life expectancy of incompetence of rheumatic origin is 20 to 30 years from its development, and effort tolerance frequently remains good until near the end. The prognosis should be based on the degree of left ventricular hypertrophy. Left ventricular failure usually occurs first and in the presence of a normal rhythm. Complications include bacterial endocarditis.

Treatment

General care should include advice in choice of occupation and limitation of physical activities. The obstetrical patient must be watched closely, and patients should be protected from bacterial endocarditis by judicious use of prophylactic antibiotics. Heart failure must be treated vigorously at its onset. No generally acceptable surgical treatment has been found as yet although

Hufnagel has placed a rigid prosthetic plastic ball valve in the descending aorta which results in increased cardiac output, diminished regurgitating volume, and a marked increase in exercise tolerance.

ACKNOWLEDGEMENT

I would like to express my sincere thanks to Dr. A. J. Kerwin for his helpful criticism of this paper.

REFERENCES

1. FRIEDBERG, C. K.: Diseases of the Heart, 1956.
2. GOULD, S. E.: Pathology of the Heart.
3. HARRISON, T. R.: Principles of Internal Medicine, 1954.
4. WHITE, P. D.: Heart Disease, 1950.
5. WOOD, P.: Diseases of the Heart and Circulation, 1956.

ESSENTIAL HYPERTENSION

M. M. FISHER, 5T8

DEFINITION

There is disagreement among investigators concerning even the definition of this condition, but a practical concept might read: essential hypertension is the manifestation of an abnormal state of circulation, diagnosed as a clinical phenomenon, if on repeated examinations the blood pressure is found to be above that considered normal for persons of similar age, race and environmental background and for which a specific etiological agent cannot be found.

The inadequacy of such a definition is not merely its negativism. The range of normal is very considerable, and the practice of making a sharp distinction between normotension and hypertension is completely arbitrary. In general an arterial blood pressure of 140 / 90 in persons under forty years of age and of 150/90 in persons over fifty is considered abnormal because persons with such pressures more frequently develop vascular disease than normotensive persons. But even an upper limit of normal pressure of 150/100 will classify as hypertensives 30 per cent of males and 40 per cent of females over forty years and a majority of males over sixty and females over fifty. There are, therefore, factors other than the elevation of blood pressure to be considered.

INCIDENCE

Fifty years ago the single page devoted to "high blood pressure" in a text of William Osler contained this statement: "One rarely finds it (the blood pressure) with the ordinary Riva-Rocci instrument above 150 mm. of mercury." In a recent issue of the New England Medical Journal Paul D. White referred to hypertensive disease as one of the two "cardiovascular diseases that have risen to a seriously epidemic level in our midst".

Although the available statistics are usually from single sources using varying criteria of diagnosis, 8–10 per cent of the American population is the figure most commonly cited while a more conservative 6 per cent does not belittle the issue It is an all too common disease affecting thousands in Canada alone.

It appears to be largely a disease of Western civilization.

PATHOGENESIS

The basic mechanism producing the increased arteriolar tone characteristic of essential hypertension is most obscure at the present time. If there is any solidarity at all among investigators about the pathogenesis of this disorder, it is that the immediate cause of the elevation in blood pressure is an increase in peripheral vascular resistance.

Recent experimental evidence points directly to the probability that arterial and arteriolar sclerosis of the benign phase of essential hypertension is primary, and precedes the development of the elevation in blood pressure. That elevated blood pressure by itself may cause arteriosclerosis is rendered somewhat dubious by the failure to find evidence of intimal arteriosclerosis in the vasculature proximal to coarctation of the aorta or in an individual with a pheochromocytoma in which the hypertension is persistent and often markedly high.

There is a strong suggestion that nervous vascoconstrictor influences play a primary role. The predisposition to hypertension is an hereditary trait transmitted as a dominant characteristic and manifested by a reaction to environmental stress by means of vasospasm. The continued stress of pressure upon this sensitive vasculature leads to structural changes in the small blood vessels. Such changes in the kidneys, and possibly the adrenals, may lead to the appearance of a second humoral mechanism which may in turn come to dominate, both from an etiological and therapeutic point of view, the original neurogenic factor.

There is also reliable evidence supporting the hypothesis that some cases at least of this disorder could be caused by a state of mild chronic aldosteronism established on the basis of a high potassium intake, of stress and anxiety, or of some yet unknown factor.

For the present at least the basic concept in the full appreciation of the hypertensive patient is that the elevation of blood pressure is essentially a symptom, not a specific disease entity, and that "essential hypertension" as it is now known will some day be separated into disease states of diverse etiology. To in part dampen this note of optimism is the sobering reflection that not one new concept of note to explain the physiopathology of hypertension has been proposed in the last fifty years.

Pathology

Essential hypertension is basically a disease of the arteries and arterioles with the functionally significant alterations occurring in the heart, kidneys and brain.

vessels

1. hypertensive arterial sclerosis

A. *Diffuse Arteriolar Sclerosis*

This involves two principal alterations:

(a) *Hyaline degeneration*: A sharply defined, smooth, acidophilic thickening of the subintimal tissues of the smaller visceral arteries is seen. This change, which may eventually involve the whole thickness of the vessel wall, is a constant finding only in the kidneys. That is, only in the kidneys does hypertension seem to be an essential factor in the production of arteriosclerosis.

(b) *Elastic hyperplasia*: There is also a splitting into several layers of the internal elastic lamina, especially of the larger arterioles and medium sized arteries but to some degree even in the smallest vessels. Later the change may involve the media also until eventually the muscular type arteries become elastic in nature and little more than passive conducting tubes.

The above changes, apparently the reaction to gradually increasing and prolonged hypertension, may be widespread, but are functionally important only in the kidneys and brain where thickening of the vessel wall and consequent narrowing of the lumina leads to ischemic changes.

B. *Effect on Larger Vessels.*

The larger vessels of the body become moderately and diffusely en-

larged as a reaction to long standing hypertension; hence, the "unfolded aorta", the "kinked carotids" and the "rubbery and tortuous limb arteries".

The progression of the condition to the "malignant" phase produces lesions characteristic of that phase but often the distinction is not marked. Here also there are two principal alterations:

(a) *Arteriolar necrosis:* This change, in which the whole thickness of the vessel wall becomes necrotic and structureless, is seen as an indistinctly limited, diffuse, eosinophilic staining area. Hemorrhages are common, and aneurysms sometimes form. This finding presents itself only in about 20 per cent of cases.

(b) *Cellular hyperplasia*: The arteriole walls become thickened by concentric "onion skin" cellular proliferation, often most marked in the media.

It is important to realize that the development of arteriosclerosis does not parallel either the degree of hypertension or its duration.

2. ATHEROMA

The relation of hypertension to this pathological entity is difficult to assess. Boyd feels that hypertensive disease often has a causal relation to atheromatous changes in the coronary arteries and probably also in the cerebral arteries. There is as yet no experimental evidence that atheromatous changes are a consequence of hypertension. Perhaps the latter process merely accelerates the degenerative changes of the former.

HEART

The increase in peripheral resistance leads to hypertrophy of the left ventricle, with increased weight of the heart and an increased rigidity of its walls. This apparent response to increased work is not proportional to the degree of hypertension present. The heart may remain compensated for many years, but commonly the left ventricle begins to fail and dilatation of that chamber occurs. This in turn produces pulmonary congestion, right ventricular hypertrophy and general venous congestion, and is the most frequent cause of hypertensive deaths.

As suggested above coronary artery disease is more frequent and more severe in hypertensives, the increased intravascular pressure apparently accelerating the ageing process in those arteries.

KIDNEYS

Some investigators feel that hypertension does not occur unless and until the kidneys are affected by vascular disease. Others, notably Bell, realizing that hypertension may develop in the absence of renal arteriosclerosis, feel that the two processes are independent in origin, but intensify each other. Approximately 10 per cent of hypertensives who die of their disease die in renal failure.

In the kidney, and probably only in the kidney, the degenerative and fibrotic changes accompanying hypertension and the subsequent gross pathology are determined by the duration and intensity of the hypertensive process. The organ may be normal in its gross appearance; it also may be the small, hard, granular "primary contracted kidney" with its finely nodular, mottled surface, irregularly atrophic cortex and distorted vascular markings. These are only the extremes.

BRAIN

Hypertension accounts for 75 per cent of spontaneous intracranial hemorrhages. These are due to the rupture of diseased arteries in the subcortical white matter, usually the "capsules", the pons or the cerebellum.

The other lesions commonly encountered are ischemic changes of variable severity, running the gamut from

miliary infarcts to large areas of encephalomalacia.

Conclusion

Although the anatomical changes associated with hypertension have been the subject of study for more than a century, the causative relationship between the vascular disease and the hypertension still remains to be established.

Patient Evaluation

In evaluating these patients one must first establish the diagnosis of hypertensive disease. One must not rely on a single blood pressure reading or two, for prolonged periods of normotension occasionally occur spontaneously, particularly during the early phases of the condition. The diagnosis is suspected when diastolic pressure greater than 90 mm. of mercury is found, and it becomes increasingly probable the more often this occurs. Diagnosis should be reserved until critical judgment has excluded pressure lability, complicating emotional factors and the expected degenerative changes of ageing.

Then it is the primary obligation of the physician to rule out as confidently as possible any specific lesion, possibly amenable to specific therapy, responsible for the condition. The diagnosis of "essential" hypertension is one of exclusion.

Finally one must evaluate the degree of hypertension present, its duration, rate of progression, and the extent of damage in the vessels, heart, brain, kidneys and retinae.

Symptoms

One encounters two types of headache in these patients; first, a "tension" headache produced by the sustained contraction of skeletal muscles and second, a vascular headache. This latter is a deep, dull and diffuse ache, usually intermittent and characteristically throbbing, especially at its onset. It may be generalized, occipital, or unilateral, commonly worse in the early hours of the morning, reaching peak intensity shortly before rising and tending to wear off as the day progresses. Neither type is related to the actual level of blood pressure. Moreover, a subjective symptom as common as headache is difficult to assess, and some observers deny the very existence of a "hypertensive headache".

Epistaxis and intermittent hematuria are also frequently encountered.

Most of the symptoms of these patients are non-specific and often are evoked during stress, that is on an emotional basis, as an adaptive or protective mechanism. Muscle stiffness, backache, generalized aches and pains, dyspnoea and constipation are common and it is an error to put much reliance on the patient's account of his symptoms.

Family History

There is often a familial tendency in the rising systolic pressure with advancing age (on an arteriosclerotic basis), in the hyper-reactivity of patients with very labile blood pressure and in cases of serious hypertensive disease. Moreover, as White points out, in some families current therapy is less effective than in others, and some families inherit heart muscle and vascular tissue that can more stoutly resist than can that of other families the hypertension they also inherit.

Prognostication

The problem of prognostication for the individual case is fraught with hazard, for within this "majority" group of essential hypertensives there is a wide variation of clinical course, based at least in part on the marked individual variation in tolerance. A patient's hypertension may not interfere at all with a long active and healthy life. Yet it may

follow a downhill course rapidly to a fatal termination, and between these extremes lies an infinity of intergrades. No one will deny that it is a disorder with serious consequences and by accelerating the normal arteriosclerotic degenerative processes reduces the life expectancy of these patients. But the average span of the disease is twenty years and two established facts must be borne in mind: first, the casually recorded blood pressure in the office or clinic bears depressingly little correlation with the symptoms, rate of progression or subsequent development of complications in the individual case. In general the danger of vascular complications and death increases directly with the height of the blood pressure, but this is on a statistical basis—very high diastolic values or progressive increase in the arterial tension over a relatively short period of time are not individually less favourable. Second, about 75 per cent of hypertensives die of diseases completely unrelated to their hypertension. One doubts the value of making a prognosis —a prognosis which could have a detrimental effect on the patient himself and which at best is most unreliable.

Management

1. selection of the patient

Not all hypertensives need be treated. The majority are asymptomatic and these patients, recognized during routine examination, with their diastolic pressure only moderately elevated (less than 100 mm. of mercury) and their symptoms minimal, present a very special problem. It has been well established that an interest by the physician in the feelings, attitudes and life situation of the patient with essential hypertension will reduce or eliminate many of his nonspecific symptoms. Certainly intensive therapy is not indicated—firm reassurance, steady encouragement, dietary management and mild sedation to ensure adequate rest will probably suffice. The patient must realize that the condition is comparatively benign and may persist for years without disagreeable happenings, that suitable therapy is available if and when required, and that frequently no specific therapy is necessary. Neither the doctor nor the patient should be mislead by blood pressure readings, the clinical significance of which may be nil.

However, the more severe varieties of the disease demand specific therapy. Statistically a high diastolic pressure shortens lifespan and a lowering of that pressure is therefore justified. Nor should specific therapy be withheld until the more or less irreversible changes have occurred.

In general, therapy is reserved for patients with definite evidence that their cardiovascular system is not tolerating the sustained level of hypertension and for the patients with severe symptoms due to their hypertension. The patient with malignant hypertension or with congestive heart failure on a hypertensive basis should of course be treated vigorously, as should the patient with hypertension of relatively short duration (under eight years) who shows evidence of cardiac or renal involvement or marked changes in the optic fundi (grade three or four). On the other hand the elderly patient with a long history and minimal evidence of hypertensive disease is best left free of dietary and drug restrictions.

2. establishment of a base-line period

If progression of the disease is not precipitous, it is of advantage to make frequent observations over a period of several weeks of the blood pressure and the clinical status of the patient, the efficiency of his heart and kidneys, and his retinal grading before drug therapy is instituted. This period will give the physician an opportunity to exclude curable forms of the disease, to evaluate the emotional and psychosomatic factors

involved, the nature and severity of the hypertensive process and the necessity for and nature of therapy. This period of observation becomes increasingly important as one deals with patients closer to that nebulous line dividing the hypertensive from the normotensive.

3. Diet

Although the value of any form of dietary restriction remains to be established, it is generally conceded that obesity should be corrected. This may lower the pressure, especially of a mild hypertensive, to a pronounced degree.

Experiment perhaps justifies the sparing use of salt. Clinically, success more often comes in the wild, fluctuating type of hypertension than in the severe cases with a very high diastolic pressure. Sodium restriction (less than 500 mgm./day) appears to retard the deterioration processes, to reduce the frequency with which essential hypertensives pass into the malignant phase and to potentiate certain hypotensive agents. To be effective the restriction must be drastic, yet care must be taken to avoid salt depletion and the aggravation of pre-existing renal impairment. It is definitely a useful adjunct to other forms of therapy, but certainly is not sufficient of itself.

4. Drugs

Hypotensive therapy is undertaken on the assumption that a prolonged marked elevation of blood pressure is in itself harmful. Evidence in support of this hypothesis is hardly overwhelming.

A hypotensive agent might effectively act by reducing either the peripheral resistance or the cardiac output. To reduce the latter would be hazardous in most cases and disastrous in many; hence, these agents must produce their effects by altering the peripheral resistance mechanisms, and consequently their effects upon the circulation in general must be considered. Ideally such an agent should reduce the blood pressure while improving renal circulation and without producing an increase in coronary or cerebral circulation or in cardiac output. Needless to say such an agent has not yet been found.

(a) *Veratrum Alkaloids*

Unfortunately the margin of safety with respect to the appearance of toxic side effects is often small or nil and the hypotensive effect, occurring as it does only in a minority and then only intermittently, is probably not significant enough to justify the prolonged use of these agents. They may, however, be used to advantage parenterally in the control of acute hypertensive situations, for example, hypertensive encephalopathy or pulmonary oedema.

(b) *Rauwolfia Compounds* (*Reserpine*)

This popular agent is felt by many to be the first used and the last dropped in therapy. Though its mode of action is obscure, it has moderate hypotensive activity, and is well tolerated for long periods. It is, therefore, particularly useful in the milder varieties of hypertension, especially in the young labile hyperkinetic patient, and also in combination with other agents, appearing as it does to have an additive, if not synergistic, effect with veratrum and the ganglionic blockers.

Toxic symptoms are relatively uncommon and postural hypotension seldom occurs. But occasionally a psychiatric syndrome is produced ranging from increased anxiety and restlessness through a variety of intergrades to a major depression requiring prolonged psychiatric care. This latter complication has dulled much of the enthusiasm which ushered in this agent.

(c) *Hydralazine* (*Apresoline*)

This is an orally effective hypotensive agent of moderate potency, found to be more effective in the milder varieties of the disease. Effective doses frequently produce distressing side effects, and a

significant lowering of blood pressure for any considerable length of time is possible only in a small minority of cases. Sooner or later severe headache, palpitation, nausea and vomiting, abdominal cramps and eventually a syndrome resembling rheumatoid arthritis and then disseminated lupus erythematosus appear, and frustrate all hopes of long-term therapy.

Though its present use is largely as an adjunct to other agents, its greater value may lie in the treatment of encephalopathic episodes.

(d) *Ganglionic Blockers*

These blockers of synaptic transmission at the autonomic ganglia are the most potent agents presently available, too potent in fact for the asymptomatic or mild hypertensive. The hypotensive effect is produced by a decrease in the total peripheral resistance in the vascular bed, augmented by venous dilatation and a pooling of blood in the venous system.

Too frequently, however, significant hypotension for an adequate part of the day is obtained only with doses producing intolerable side effects, the result of widespread autonomic inhibition. Most troublesome of these are the effects of parasympathetic blockade (constipation, dry mouth, tachycardia, urine retention, cycloplegia and hypotensive episodes). Thus, these agents should be given only when the consequence of a high diastolic pressure appears distinctly menacing, as in grades 3 and 4 retinopathy, encephalopathy, intractable headache, congestive heart failure or vascular accident, which has not responded to the usual, more conservative regimen.

(e) *Adrenergic Blockers*

These agents have a direct action on the smooth muscle of the arterioles, thereby preventing sympathetic vasoconstriction. Though effective in lowering the blood pressure of a considerable number of hypertensives, their administration is not yet practicable, due in part to an unfortunate increase in cardiac output.

(f) *Pyrogens*

This therapy involves a vigorous program of rigor and fever for six days a week until the disease shows evidence of abating, usually in three or four months. There is a coincident restriction in sodium. The process is difficult, the patient must be stoical, and there are more effective methods available. Hence, it has almost completely been dropped from the therapeutic program.

(g) *Drug Combinations*

With so many possible sites of action it seems obvious that a community effort on the part of the various agents would produce a more marked hypotensive effect than would any agent by itself. And such was the case with several combinations. But many now feel that the dangers increase hand in hand with the hypotensive effects and that all the characteristic toxic reactions of each drug in the combination still appear. This aspect of the therapeutic program is still too embryonic to evaluate.

Drug therapy is the best treatment to date, but cannot be considered as yet to be a satisfactory answer to this most difficult therapeutic problem. The drugs are costly; a patient's weekly bill might be in the neighbourhood of twenty to thirty dollars. But more importantly the control is difficult to maintain, impossible in fact without an intelligent, cooperative patient and even under the best of circumstances can but be considered inadequate.

5. SURGERY

Sympathectomy should be reserved until all conservative measures have failed. It is a major operation which can and often does produce protracted disability and which produces significant

results only in a minority. But the true value of the operation is difficult to assess, for it has been used somewhat indiscriminately on all varieties of hypertension. Brilliant results have been obtained in some cases, but as yet there is absolutely no way of selecting those patients who will so benefit by the procedure. Surgery is not likely to be the therapy of the future.

Conclusion

The problems of "essential" hypertension are complex and manifold. Much has been solved, but much more remains a mystery.

Acknowledgement

The author pleads guilty to the most blatant plagiarism, and wishes to express his sincere appreciation for the interest shown and orientation given by Dr. D. B. Moran.

Bibliography

Harrison, T. R.: Principles of Internal Medicine, 1954.
Ball, C. T.: Symposium on Hypertension, U. of Minn. Press.
Schroeder, H. A.: Hypertensive Diseases, 1953.
Practitioner, **166**: June 1951.
New Eng. Med. Jour., **248**: May 21, 1953; **256**: May 23, 1954.
Can. Med. Assoc. Jour., May 15, 1956; Oct. 15, 1956.
Br. Med. Jour., Nov. 3, 1956; Nov. 24, 1956.
Medical Clinics of North America, Sept. 1956, January 1957.

CASE REPORT: DISSECTING ANEURYSM

R. HERST, 5T8

History

THIS 66-year-old male had been well until 8.30 p.m. on the night of admission when he was suddenly seized by a severe sharp substernal pain as he was walking toward his desk. He did not recall whether the pain radiated, but remembered that he felt extremely unwell and that his legs were numb and tingling. He collapsed and was brought to the Emergency Department of the Toronto General Hospital half an hour after the onset of the pain.

History of past health revealed a cholecystectomy two years ago. For the past one year the patient had had frequent bounts of epistaxis, and had been treated by an outside doctor with iron, liver and Vitamin B_{12} for anemia. About two weeks prior to admission, the patient suffered an episode of midsternal pain lasting all day, but it was not severe enough to prevent him from working. He also had had occasional bouts of gnawing epigastric pain occurring in mid-morning and afternoon, for which he took neither food nor alkali, and which resolved spontaneously.

Physical Examination

Examination revealed a cyanosed, acutely ill, elderly man with a left lower facial paresis. His pupils were regular, equal, and reacted to light and accommodation. The fundi exhibited some arteriolar narrowing, but were otherwise normal. There was jugular venous distension to the angles of the jaws, and the right carotid pulsation was greater than the left. The chest was clear. The heart was regular at a rate of 50 per minute; the blood pressure was 100/60 on admission, but had fallen to zero an hour later. The heart sounds were faint; no murmurs were present. The patient held his abdomen rigidly, but could be made to relax by diverting his attention; liver and spleen were not enlarged. Rectal examination revealed slight prostatic enlargement with no associated tender-

ness. There were good, equal femoral pulsations. The dorsalis pedis and posterior tibial pulsations were not palpable. There was no oedema and no clubbing. Neurological assessment revealed a drowsy but cooperative, somewhat apprehensive patient. There was evidence of facial nerve involvement on the lower left side. Motor power was good in the arms and legs. The reflexes were equal but sluggish; the plantars were downgoing.

Differential Diagnosis

1. Myocardial infarction.
2. Dissecting aneurysm of aorta.
3. Perforated peptic ulcer.

Course

January 17

9.00 p.m. Admitted.

10.00 p.m. Patient was given morphine and oxygen by nasal catheter. The blood pressure was zero and Levophed, 4 cc. in 1000 cc. of 5 per cent glucose in distilled water, was started intravenously.

11.00 p.m. Further constricting midsternal pain relieved by morphine sulphate gr. $\frac{1}{2}$ I.V.

11.30 p.m. 100 cc. of the intravenous had run through, and blood pressure was 80/60.

12 midnight. Pressure maintained at 80/60. Laboratory tests done up to this point revealed haemoglobin 90 per cent, WBC 16,000, ESR 10 mm., and blood sugar prior to the intravenous 119 mgm. per cent. Urinalysis showed acid reaction, specific gravity 1018, albumin trace, and many red blood cells on microscopic examination. ECG showed sinus bradycardia with no evidence of recent infarction.

A surgical consultation was requested because of the possibility of a perforated ulcer. The surgeons did not feel this was a likely possibility, but suggested a flat plate of the abdomen.

January 18

2.00 a.m Flat plate showed no free air. Chest X-ray showed a tortuous thoracic aorta. Patient felt better.

3.00 a.m. Blood pressure left arm 90/70; right arm 70/50, a grade 1 bruit was heard over the right common carotid and a grade 3 bruit over the left. The left carotid pulsations were less than the right.

10.00 a.m An aortic diastolic murmur was heard for the first time. Blood pressure remained steady at 90/70.

Patient's total urine output during the first 24 hours after his attack was 80 cc. His chief complaint at this time was weakness. He was still critically ill.

January 20

The patient was feeling well at 7.00 a.m. At 7.30 a.m., however, he suddenly became dyspnoeic, and his face and shoulders became a blue-black colour. The patient expired within a few minutes.

Autopsy Findings

At autopsy there was a dissecting aneurysm of the ascending aorta which extended along the left common carotid artery. The aneurysm had ruptured into the pericardial sac which contained 400 cc. of fresh blood, death being due to cardiac tamponade. The heart weighed 390 grams. The auricles were of normal size, lined with smooth grey endocardium, and filled with dark red fluid blood. The valves were normal, the cusps thin and freely movable with thin, thread-like chordae tendineae.

The coronary arteries were normally distributed, the intima of both right and left vessels was dotted by small yellow atherosclerotic plaques. There was no stenosis or calcification of either coronary artery.

The aorta was dilated and measured 10 cm. in circumference 5 cm. above the aortic ring. The outer surface was dark red and soft; the intima was dotted with

small atherosclerotic plaques. Two centimeters above the aortic ring on the posterior wall, there was a small vertical intimal tear, 1 cm. in length, and distal to this point the wall of the aorta had undergone dissection. The media had split, and there was a small amount of fresh and clotted blood between the layers. The dissection extended completely around the aorta and distally to a point 3 cm. beyond the origin of the left subclavian artery. The dissection was compressing the lumen of the left common carotid artery. About 1.5 cm. above the aortic ring, the outer layer of the media was perforated, the dissection going through the adventitia and pericardial reflexion, thereby rupturing into the pericardial sac.

Microscopic examination of the point of rupture showed an area of atheroma extending into the media, and producing secondary medial necrosis. The aneurysm was felt to be primarily due to the ulceration in the atheroma.

Discussion

Dissecting aortic aneurysm occurs predominantly among males between the ages of 40 and 70 with pre-existing hypertension. It can, however, occur in young adults, especially in association with pregnancy and coarctation of the aorta. Weakness of the media due to degenerative disease is the basic disturbance. Rupture of branches of the vasa vasorum causes a tear through the intimal surface, and permits subsequent dissection by the main aortic blood stream along the outer layers of the diseased media. The intimal tear occurs commonly a few centimeters above the aortic valve or near the origin of the left subclavian artery, but it may occur anywhere in the thoracic aorta.

Death is due usually to a perforation of the aneurysm through the adventitia into the pericardium with subsequent hemopericardium and cardiac tamponade. The aneurysm may also perforate into the left pleural cavity or more rarely into the mediastinum, right pleural cavity, pulmonary artery, or into the abdominal cavity by way of the retroperitoneal tissues. Occasionally the dissection may lead back through a second intimal perforation into the original aortic lumen, and thus recovery is possible, but even this healed channel is subject to subsequent rupture.

While many of the symptoms of dissecting aneurysm resemble those of acute myocardial infarction, a difference in blood pressure in the arms favours dissecting aneurysm. Repeated examinations often reveal changes in the pulses in aneurysms. In both conditions there is severe retrosternal or precordial pain, but the pain of dissecting aortic aneurysm usually occurs more suddenly, is often of a tearing quality, and is apt to have more widespread radiation to the back of the head and neck, the posterior thorax, the lumbar region, the epigastrium or the lower extremities. Syncope, nausea and vomiting, dyspnoea and cold clammy extremities are common to both, but with dissecting aneurysm temporary loss of vision, numbness in upper or lower limbs, paralysis of an extremity or transient changes in reflexes are more common. There may be signs of aortic insufficiency not previously present, or of a left pleural effusion. Pulsations may be absent in branches of the subclavian or iliac arteries. Roentgenologic examination sometimes discloses a distinctive progressive widening of the aorta. Absence of typical electrocardiographic changes of acute myocardial infarction is a critical differential diagnostic feature. Occasionally a dissecting aortic aneurysm may produce myocardial infarction by extending along a major coronary artery, thereby forming a hematoma, the pressure of which occludes the lumen.

PRINCIPLES OF RADIATION HAZARD CONTROL

J. HOFFMAN, 5T9

Introduction

At the Chalk River Atomic Energy Project, medical research is investigating a relatively new aspect in the broad field of "poisoning". It is new inasmuch as chemical toxicity has been replaced on the molecular level by a type of tissue damage due to atomic nuclear activity best explained in physical terms.

For a clear perspective of this topic, certain background information is essential. There are four reactors or "piles" at the Project, known as ZEEP, PTR, NRX and NRU. NRX and NRU are the largest, and from these two stem most of the hazards with which we are concerned. Without delving into the details of their operation, we shall find it sufficient to say that those who handle the equipment may, on occasion, be exposed to external (skin) or internal (pulmonary or gastrointestinal) contamination by radio-active chemical components of fuel rods such as uranium metal and plutonium, of control rods such as boron and bismuth, of irradiated samples such as cobalt 60, iodine 131, actinium, thorium and radium, and by fission and decay products such as strontium and cesium.

Each of these substances, whether in elemental form or in chemical combination, undergoes its own, spontaneous nuclear decay scheme with characteristic half-life and alpha, beta, or gamma emission carrying an associated energy of definite value. An alpha particle is really a helium nucleus, composed of two protons and two neutrons. A beta particle is an electron, generally ejected from an atomic nucleus with a large neutron excess, a given neutron disintegrating into a proton, an electron, and a tiny uncharged particle of negligible mass called a neutrino. Gamma rays are the same as "hard" or short wavelength X-rays. There are four radioactive series—thorium, neptunium, uranium, and actinium—within which the natural occurring radioelements distribute themselves.

Of major importance are the instruments used for estimating radiation. They may be designed as *scintillation counters*, based on the principle that a photon or particle of high energy radiation striking a phosphor-coated screen ejects a photon of light in the visible region which can then be detected by a photoelectric cell (usually a photomultiplier tube), or as *Geiger counters* for beta, gamma, and X-rays whose ionizing effects in a gas at low pressure within the chamber cause an electric discharge or pulse which will activate an electric counter. The count obtained will generally be proportional to the mass of the radiochemical.

Biological Implications

Our interest here centres around the biological significance of radiation. Radiochemical poisoning exerts its effects in a comparable manner to X-rays, and although the chemical behaviour of the isotope will determine how the body handles and excretes it, which organs will contain the greatest concentration, and consequently the particular part subject to greatest radiation damage, the truth is that most of these radioisotopes are chemically and pharmacologically completely innocuous in these minute submicrogram quantities. Natu-

---

Ed. note: Much of the physical data as presented in the original manuscript has been deleted because of the highly technical terminology involved.

ral uranium, the one exception, can cause kidney damage at excretion levels close to those which are radiotoxic.

In acting upon individual body cells, the basic change caused by beta, gamma, and alpha rays is ionization of cellular constituents. Since alpha and beta rays are charged particles, it is apparent that their passage through tissue will disrupt the outer electron shells of neutral atoms by either removing an electron or adding an extra one. Gamma rays, too, produce ionization, but through a different mechanism because they are not charged particles but rather photons of electromagnetic radiation of short wavelength. The energy of these photons may be absorbed in tissues in the following ways. First, a gamma ray striking an atom may be absorbed and result in the removal of an orbital electron (photoelectric effect); second, if it strikes an orbital electron the incident ray may be only deflected and proceed at a lower quantum energy, the orbital electron being ejected from the affected atom (Compton effect); and third, "pair production" may occur, in which the gamma ray effectively converts its energy into mass and becomes a positron and negatron. The probability that any one of these three processes will occur depends upon the energy of the incident gamma radiation.

What harm can such ionization do? As a consequence of ionization within a somatic cell's nucleus, the cell may undergo changes represented, for example, by increased keratinization of irradiated epidermis; or the cell may degenerate and liberate "H-substance" so that there will be an erythematous reaction. Genetic changes may occur as a result of irradiation of germ cells, in which damage to genes or disruption of the linear structure of individual chromosomes are the main features. A chromosome whose normal alignment has been broken may reconstitute itself, but quite possibly with the wrong ends apposed or with a fragment of a different chromosome; hence, a mutation results. The magnitude of these alterations depends upon the total roentgen dose (energy) absorbed by the tissue over the period of exposure, i.e. the biological effect is cumulative. It must be noted, however, that an important difference exists between dose received and dose absorbed, for any fraction of the radiation which passes completely through a tissue without giving up its energy produces no ionization and, therefore, no biological changes.

The clinical manifestations of irradiation may be immediate or delayed. Acute exposure to 25 r has no immediate effect, but 25 to 50 r cause a transient lymphocytopenia and neutropenia; one of the most sensitive biological indications is a fall in platelet level. At 50–100 r, significant blood cell changes may occur, besides nausea and vomiting in about 2 per cent of persons; in addition there is a delayed effect in the form of a shortening of life expectancy. When the level reaches 150 r there may be about 25 per cent chemical casualties within a few hours, and at 300 r, a 20 per cent mortality in one month. Four hundred roentgens will be fatal to about 50 per cent of persons within two to six weeks, and 600 r in a day 100 per cent fatal.

Long-term possibilities of radiation exposure include (data from animal experiments mainly) shortening of life span, increased incidence of mutation, leukemia (latent period of six years) and tumors (latent period of twenty years), cataracts, cardiovascular and renal disease, sterility, and impaired growth rate. In any case the severity of the radiation injury is affected by the dose, the extent and part of the body involved, the type of radiation (alpha, beta, or gamma), and the age of the individual. Radiation is generally more effective on more complex organisms, e.g. mammals are more susceptible than insects. A dose

distributed over the entire body is worse than a dose localized, for instance, to one limb, where 4,000 r are required to cause skin cancer. Radiosensitivity decreases with age, and this applies both to entire organisms and the cells.

The genetic effects depend on total dose rather than dose rate. Chromosomal structural change is of little importance, and the death of a sperm cell, while a factor in sterility, can have no genetic consequence. It is the increased numbers of mutations in genes that are important; the types of mutation already occurring will recur with greater frequency as will new or rare types. Damage to genetic structure cannot be repaired, and it is thought that no level of radiation is too slight to exert this effect. Of course, it is only in the reproductive years of life that this matters at all. On the assumption that all naturally occurring mutations are caused by natural background radioactivity, it has been calculated that the present mutation rate would be doubled by an accumulated dose of 30 to 80 r before procreation, the relationship being practically linear.

Based on all of these hazards, the International Commission on Radiological Protection has set certain maximum permissible values for exposure to ionizing radiation, besides listing for each radio-isotope the particular organ which should be considered "critical" from the viewpoint of metabolic concentration of the radioisotope in it and the organ's susceptibility to radiation. Most sensitive are hemopoietic tissue, gonadal germ cells, and intestinal epithelium. Less so are nervous tissue and muscle.

Man has managed to increase the "background radiation" through such innovations as medical X-rays and atomic bombs. Approximate values for surface exposure to X-rays used in pregnancy are 3 to 6 r, for dental films 3 to 5 r, for chest films less than 0.05 r and fluoroscopy 3 to 20 r. Even home television sets provide us with 0.6μr/sec. Luminous dial wrist watches are estimated to account for somewhat under 1 per cent of the background level.

The exploding of an atomic bomb does damage in three ways, through the heat blast, a shock front, and radiation. Immediate radiation effects may occur from neutron bombardment of bone, making the bone artificially radioactive, and from gamma radiation. The gamma dose at 1,000 metres may reach 1,000 r, which is lethal, but the exponential decrease with distance from ground zero makes this relatively unimportant at greater distances. It is long term contamination from radioactive fallout that is significant at large distances. Among the observed effects at Hiroshima and Nagasaki have been cataracts, leukemia, and impaired growth patterns in some children, attributable in part to the initial gamma flash and in part to fallout.

Radiochemical contamination is likely to have an expanding meaning for larger and larger segments of the populace. Not only is this true because of nuclear detonations and the possibility of warfare waged with such weapons, but also because of the increasing application of atomic energy as a power supply in civilian economy. The field of transportation may see varying degrees of conversion to atomic engines, and both private industry and governments may seek electricity from atomic plants. Therapeutic uses of radioisotopes in medicine, their use in biochemistry as tracers, and their manipulation in other sciences and engineering will all tend to expose more people to potential radiation hazards. However, once the metabolism, pathological effects and dosimetry of radioactive materials become better known, industrial precautions will probably become routine and dangers minimal.

At Chalk River, it is not an easy matter to prevent and detect possible contamination of personnel. Generally,

most radiochemical work will be done in fumehoods, and precautions such as using rubber bulbs instead of oral suction for filling pipettes are taken. The Radiation Hazards Branch continually check the background count of buildings and equipment. Every employee is required to wear a badge which contains a film that blackens under exposure to radiation and is replaced weekly. Routine blood counts are done at regular intervals at the plant hospital. Lastly, in the case of employees suspected of contamination with radioisotopes, the bioassay laboratory does radiochemical analyses on urine, blood, faeces, tissue and other secretions.

Urinalysis is a good method since urine, as a biological specimen, is not only readily available, but provides sufficient volume so that the presence of submicrogram quantities of radioisotopes may be detected. Blood and faeces are only infrequently used. Urinary excretion of these elements generally follows a power function curve, and from the microcuries of activity estimated in the particular sample, allowance being made for nuclear decay while in the body, the original body dose can be calculated. Generally, a 15-hour sample is taken and a colorimetric estimation of urinary creatinine content is used as a check on the period of excretion. The aim in the chemical processing of the urine is to obtain a residue of minimal weight plated on a metal disc. The activity on the disc can then be counted. Special chemical analyses have been devised for each radioisotope, depending upon its relationships in the periodic table of elements. These same relationships can be correlated with the way in which the body handles the substance. At present, cesium 137 is one example of research in this field.

Conclusion

An attempt has been made to provide a descriptive outline of the essential features of biological radiation hazards, together with some of the quantitative aspects. It is well for the physician to be aware of these matters. As yet there is no antidote for damage caused by radioactivity.

Acknowledgement is made to Dr. C. G. Stewart, Director of the Medical Division at Chalk River, who provided much valuable information.

VAGINAL BLEEDING: PART II

P. G. WALFISH, 5T8

UTERINE bleeding associated with pregnancy may be arbitrarily divided into three main stages: early gestational, late gestational (antepartum) and postpartum.

1. Early Gestational Bleeding

This will be defined here as uterine bleeding that may occur in the first or second trimester of pregnancy due to:

A. Abortion
   i. Spontaneous
   ii. Induced
B. Ectopic Pregnancy
C. Hydatidiform Mole

Early abortion vs. ectopic (tubal) pregnancy

When a patient misses a menstrual period or is overdue a few days to several

Ed. note: The first part of this paper dealing with vaginal bleeding not associated with pregnancy appeared in the November 1957 issue of this Journal.

weeks and then begins to bleed persistently, the first thought is early gestation and threatened abortion. If the bleeding is of considerable duration, one is faced with the question of whether or not the embryo has been retained or has been expelled. However, it is often forgotten that ectopic gestation also presents the same history. In threatened abortion as with a tubal pregnancy, bleeding may be slight while in the incomplete abortion it be may rather profuse. Pain is not a conspicuous feature of early abortion, and may be absent while in tubal pregnancy attacks of acute pain usually occur in the lower abdomen on the affected side of the pelvis, accompanied by nausea, vomiting and syncope.

Pallor and rapid pulse result when internal hemorrhage occurs. With threatened abortions (20 per cent of all gestations) symptoms subside spontaneously, and the pregnancy continues in about half the cases. But with the inevitable variety, bleeding and pain increase with dilatation of the cervix and rupture of the membranes preparatory to the expulsion of the products of conception. Abortion is incomplete when any portion of the ovum has been retained. This is assumed when abnormally profuse and prolonged lochia follows.

Ultimate differentiation depends mainly on information obtained by bimanual examination. In uterine abortions, one can usually palpate at least some uterine enlargement with softening and patulousness of the cervical canal but no tenderness or palpable enlargement of the adnexal region. In a tubal pregnancy, the uterus is not obviously enlarged, and the cervix may show softening and exquisite tenderness when moving it. There is a tender unilateral mass in the adnexal region sometimes very slight and indefinite and at other times, large and unquestionable. If internal hemorrhage is extensive, a boggiess in the Pouch of Douglas will be felt.

Valuable and often decisive results may be achieved by such diagnostic procedures as pelvic puncture and aspiration, peritoneoscopy and culdoscopy. Biologic tests of pregnancy are usually not of definite importance, for they may be positive or negative for a tubal or uterine pregnancy. Estimation of progesterone levels will help establish whether or not the pregnancy is likely to continue when a threatened abortion has occurred.

MISSED ABORTION VS. INDUCED ABORTION VS. HYDATIDIFORM MOLE

If uterine bleeding occurs after amenorrhea has existed for three to six months, the above mentioned conditions, although uncommon clinically, must be considered because of the grave results that follow if not diagnosed soon enough.

Induced abortion must always be considered when a female in the reproductive era bleeds profusely from the vagina. The history is rarely reliable. Signs of trauma either mechanical or chemical in the vaginal region are usually seen. Extreme neurogenic or secondary shock often accompanied by oliguria or uremia due to kidney malfunction and a positive blood culture accompanied by a rising temperature due to puerperal sepsis are the characteristic features.

When missed abortion occurs, the dead embryo instead of being expelled is retained as an intrauterine mole beyond two months. It is not until the later stages that abnormal clinical features appear prominently. Bleeding is commonly intermittent, but consists of free gushes of blood or only a slight muddy brownish discharge when it occurs. Eventually increasing weakness, malaise, headache, nausea, decreased appetite and fever develop. Symptoms and signs of pregnancy regress or disappear. Bleeding may be so profuse as to cause death.

A hydatidiform mole is composed of chorionic villi, but there is a controversy

as to whether the abnormal process which develops is degenerative or neoplastic—the latter being more popular. It is a rare disease (1 in 2,500 pregnancies). Uterine bleeding commonly occurs between the third and fifth months of pregnancy. Usually there is a disproportionately large uterus compared to the duration of the pregnancy, unless large masses of vesicular material have already been expelled, so that the fundus may be at the level of the umbilicus although the pregnancy is only of four months duration. However, none of the positive signs of pregnancy can be demonstrated. Repeated quantitative hormonal studies of blood, urine and spinal fluid showing an increasing titre of chorionic gonadotropin are of great value in establishing the diagnosis provided that toxemia of pregnancy has been eliminated. Microscopic examination of extruded vesicular tissue will confirm the diagnosis. A malignant variety called chorioadenoma destruens which is more locally than systemically invasive may perforate the uterine wall to give fatal abdominal bleeding or metastases to the vulva, vagina and lungs.

2. Late Gestational Bleeding (Antepartum Hemorrhage)

The majority of cases are due to partial or complete separation of the placenta from its attachments to the uterine wall as in placenta previa and accidental hemorrhage. A clinical classification could then be:

A. NORMALLY SITUATED PLACENTA
(a) Accidental hemorrhage
(b) Rupture of uterus
(c) Onset of labour with more than usual amount of show

B. ABNORMALLY SITUATED PLACENTA
(a) Placenta previa

Extensive investigations to establish the location of the placenta are not always available and often are contraindicated because of their hazards. Not infrequently, therefore, a diagnosis must be made on the basis of clinical features alone.

PLACENTA PREVIA

Uterine bleeding may occur at any time from the sixth month of gestation until the onset of labour. The first hemorrhage is sudden and usually painless unless labour supervenes. In the majority of cases bleeding is slight, but even if it is profuse, it is rarely fatal. The initial bleeding may be followed by slight recurrent hemorrhage, but can be profuse and dangerous at any time.

There is an increased incidence of premature labour, malposition and malformation of the foetus. The presenting part is higher up than normal and movable. Uterine tonus and size are unaffected. The fundus is easily palpated and tenderness is absent. Fetal heart sounds are usually heard.

A boggy, elastic mass and pulsating vessels can be felt between the fornices and the presenting part. The only definitely positive sign of placenta previa is the palpation of the placenta through the internal cervical os, but this should *never* be done *unless* the patient has been placed in an operating room under sterile conditions suitable for delivery vaginally or by cesarean section and blood ready for transfusion.

Other methods of investigation have been devised in an attempt to localize the placenta, mainly by the use of such radiological methods as:

(a) Flat plate which may show the presence of calcification in the placenta.
(b) Soft tissue studies using the gravitational method.
(c) Arteriography of the placenta by injection of contrast substances (used chiefly if under 32 weeks gestation).
(d) Cystography with contrast substances—now rarely used.

These investigations will be limited by the severity of the bleeding and consequent need for immediate treatment.

ACCIDENTAL HEMORRHAGE (ABRUPTIO PLACENTA)

Vaginal bleeding tends to occur at or near the time of labour. The onset of hemorrhage may be preceded by toxemia, but very often the gravest cases occur without warning. Here we are considering the revealed type of bleeding which has little or no pain. However, bleeding may also be concealed by being retained in the uterus either retroplacentally or in the amniotic space. In such cases there is more pain, for blood is retained under tension, and separation of the placenta is more complete. Since the amount and duration of bleeding are variable, so also is the clinical picture.

Usually slight or severe abdominal pain is present. Nearly always there is tenderness of the uterus either localized or diffuse. In severe cases, the uterus is tense, hard and perhaps increased in size. Contractility of the uterus may have ceased and palpation of the fetal parts becomes difficult or impossible. Fetal movements or heart sounds are often absent.

If cervical dilatation exists, the presenting part will be felt without any displacement, and the placenta is not palpable. But since differentiation between placenta previa and accidental hemorrhage usually has not been established, it is wise to avoid vaginal examination unless the aforementioned precautions associated with placenta previa are taken.

RUPTURE OF THE UTERUS

The shock following rupture of the uterus may simulate a grave case of accidental hemorrhage, yet there is little or no vaginal bleeding. The uterus is contracted and empty, separate from the fetus. Pain suddenly ceases during labour. This condition should be particularly suspected in cases with dystocia or uterine scars.

ONSET OF LABOUR WITH MORE THAN USUAL AMOUNT OF SHOW

Show is a pink or reddish discharge from the vagina. It may occur shortly after or several days before the onset of labour. Show is only a sign of labour if accompanied by regular, intermittent uterine contractions which progressively increase in frequency and intensity. If the latter are absent, labour cannot be considered imminent.

3. Post Partum Hemorrhage

This is considered to occur when greater than 500 cc. of blood are lost at any time from the birth of the fetus or products of conception until the end of the puerperium. If it occurs within the first 24 hours, it is called primary, if later than the first 24 hours, secondary.

This complication is said to be present in 1 per cent of all deliveries and accounts for 2–5 per cent of maternal deaths.

PRIMARY POST PARTUM HEMORRHAGE

This occurs from either the placental site due to an inadequate contraction of the uterine musculature and/or an inadequate clotting of the blood, or from other areas in the genital tract due to the trauma acquired in the course of the delivery. Some of the traumatic bleeding occurs extra-utero and has been considered under extra-uterine bleeding.

A. BLEEDING FROM THE PLACENTAL SITE

Any time within several hours after delivery of the placenta, the greatest danger being in the first hour, uterine bleeding which is suddenly profuse may occur, and then continue intermittently as the uterus relaxes after each contraction, or bleeding may persist as a continuous oozing which is not usually considered serious until its cumulative

effect gives rise to signs of severe shock. The uterus may be so relaxed that it is no longer palpable through the abdominal wall or if felt, is soft and enlarged.

Etiology

i. *Inadequate contraction of uterine musculature (atony)*

(a) Uterine inertia—due to overdistension of hydramnios, multiple pregnancy, exhaustion of prolonged labour, lax abdominal muscles, excessive anaesthesia and analgesia.

(b) Adherent and retained placencental fragments—due to failure of the normal mechanism of placental separation.

(c) Improper or premature efforts to deliver the placenta as in precipitous labours or operative deliveries.

(d) Antepartum hemorrhage—due to placenta previa or abruptio placenta.

(e) Inversion of uterus.

(f) Pelvic neoplasms especially fibroids.

(g) Overdistended bladder.

(h) Idiopathic.

"Uterine atony is the causative factor in almost 50 per cent of all grave postpartum hemorrhages and the atonic condition of the uterus after placenta previa and abruptio placenta is responsible for one-half of the remainder".[1]

ii. *Inadequate clotting ability of the blood*

This condition should always be suspected when a patient with postpartum hemorrhage continues to have unclotted blood oozing forth from the vagina in spite of all adequate therapeutic measures to counteract the hemorrhagic shock and traumatic injuries and a tonic, contracted uterus still exists.

(a) *Conditions related to pregnancy*:

It is known that transitory abnormalities in the clotting mechanism at or near the time of parturition can be responsible for uterine and generalized bleeding. At term, clotting and bleeding times are usually normal, but when labour occurs, there is normally a decrease in the plasma concentration of prothrombin, fibrinogen, proconvertin and an increase in plasma fibrinolysin activity.

Hypo- or afibrinogenemia is associated with such clinical conditions as abruptio placenta, macerated fetus and retained products of conception, amniotic fluid embolism, severe toxemia of pregnancy, and septic induced abortion.

Peculiar hemorrhagic disorders may occur due to the presence of a plasma anticoagulant.

The exact mechanism is not known, but it has been shown clinically that when the plasma fibrinogen level is 100 mgm. per cent or less general hemorrhagic symptoms can occur in addition to uterine bleeding. The postulated mechanism of this is that in the above mentioned conditions tissue thromboplastin derived from decidua, placenta, or amniotic fluid gains entrance to the maternal circulation. This thromboplastin combines with prothrombin, proconvertin and calcium to produce thrombin which in turn combines with fibrinogen to form microscopic fluid emboli distributed mainly in the liver and lungs. This intravascular coagulation phenomenon results in a lowering of plasma fibrinogen. In addition there is believed to be an increase in activity of the antagonistic (anticoagulative) mechanism, thereby further aggravating the coagulation defect. If the plasma fibrinogen level falls within the range of 60–100 mgm. per cent or less, defective clotting will occur.

The second cause mentioned, namely, a powerful plasma anticoagulant, is based upon a clinical picture occurring within a few months of pregnancy very similar to hemophilia with severe bleeding into the joints and soft tissues. An

increased clotting time of venous blood but a normal prothrombin time are found. It is, therefore, postulated that there is an immune mechanism related to the fetus giving rise to a circulatory anticoagulant resulting in an abnormal bleeding tendency.[6]

(b) *Conditions unrelated to pregnancy*: Thrombocytopenic purpura (idiopathic and drug sensitivity) in pregnancy is not different from that when pregnancy is absent giving such signs as a generalized bleeding tendency, purpura, increased capillary fragility, a decreased platelet count, prolonged bleeding time and poor clot retraction.

Hypoprothrombinemia due to liver disease or vitamin K deficiency may also occur.

B. UTERINE BLEEDING FROM SITES OTHER THAN THE PLACENTA

This will include traumatic injuries during labor to the cervix and uterus. The etiology of trauma to these areas may be classified as follows:

(a) Assisted deliveries e.g. forceps, version, caesarean section.

(b) Improper management of the 2nd stage of labor e.g. precipitous labour.

(c) Dystocia between passenger and passages.

(d) Induced abortion either self or criminal.

(e) Previous pathology, lacerations or surgery involving the uterus.

Trauma to the cervix consists mainly of laceration and evulsion which give rise to increasing bleeding after delivery but which progressively decreases when some degree of clotting begins. It can be controlled by immediate suture; and can be readily diagnosed and treated by routine inspection.

Two important traumatic conditions occur in the uterus, namely, rupture and inversion.

Rupture of the uterus gives rise to a considerable degree of shock and a variable amount of bleeding. Abdominal pain may be obscure or suddenly severe with a tense abdomen suggestive of peritoneal irritation. The lower uterine segment is locally tender and thinned out. The fundus is firmly contracted, but the ring or zone of retraction is abnormally elevated to almost the level of the umbilicus. The cervix is edematous and pulled into the abdomen, and the vagina is taut.

If rupture of the uterus is incomplete, bleeding may precede shock for a considerable period of time and so can only be detected early by exploration of the uterus for lacerations.

Complete or partial inversion of the uterus commonly occurs as a result of poor management of the 3rd stage of labor due to traction on the umbilical cord or attempts to express the placenta while the uterus is relaxed. However, it may occur spontaneously or due to a congenitally short umbilical cord. There is usually profuse bleeding and profound shock during or after the third stage of labor. Shock is at first out of proportion to the hemorrhage. Later the blood loss will increase the severity of shock and unless large transfusions are given, will progress to irreversible shock.

Absence of the uterus above the pelvic brim (complete inversion) or only a cup-shaped indentation of the fundus (partial inversion) can be felt on abdominal examination. The presence of a large roughened bleeding mass in the vagina suggests a pedunculated tumor, but careful inspection may reveal the Fallopian tubes.

SECONDARY POST PARTUM HEMORRHAGE

The most common etiological factors are:

(a) Retained fragments of placenta.

(b) Faulty involution of the placental site.

(c) Fibroids with or without degeneration.

(d) Septic endometritis.

Retained fragments of placenta (or products of conception) constitute one of the most common causes of uterine bleeding. It occurs after abortion either spontaneous or induced and full term deliveries. In some cases considerable masses of placenta are retained for long periods of time with little or no bleeding while in others a few small particles can be associated with prolonged and profuse bleeding. However, symptoms of retained placental fragments usually appear soon after the end of the first week and since the lochia is quite normal prior to the appearance of bleeding, the hemorrhage is quite unexpected. The initial loss of blood is frequently considerable, but repeated episodes of lesser bleeding are just as dangerous.

In septic endometritis, the post puerperal patient is usually febrile with a tender and sub-involuted uterus. There is often a cessation or diminuation of the lochia whose character varies with the causative organism. It is likely that severe bleeding is ultimately related to a coagulation defect resulting from decreased plasma fibrinogen. Retained blood clots and fibroids with or without degeneration must also be considered.

In any case where secondary post partum hemorrhage is considerable, exploration of the uterus under strictly aseptic conditions is indicated.

Acknowledgement and bibliography appear after Part I, **35**: 1, 1957.

ANSWERS TO "ON INSPECTION"

R. C. BULL, 5T8

FIGURE 1. This is a neoplasm of the thyroid, the diagnosis being based on the size and location of the mass. A thyrotoxic goitre could be considered, but these are always uniformly bilateral.

A complete structural classification (by tissues) appears in Post graduate Medicine, **22**: No. 4, Oct. 1957, and a similar type is in Perkins' Surgery (Livingstone). This book by Perkins is an essential part of every student's library ($1.70).

A classification by location, however, is very practical.

1. SINGLE
   - A. MIDLINE
     1. Submental glands.
     2. Thyroglossal duct cyst (up and down with swallowing).
     3. Adenoma of isthmus.
     4. Ectopic (lingual) thyroid.
     5. Dermoid.
     6. Goitre.
   - B. LATERAL
     1. Benign thyroid adenoma.
     2. Benign salivary gland tumours.
     3. Branchial cleft cyst.
     4. Cystic hygroma.
     5. Pharyngeal pouch.
     6. Carotid body tumour.
     7. Cervical rib.
     8. Inflammatory lesions: tuberculosis, actinomycosis, boils.
     9. Soft part tumours.
     10. Vagus neurofibroma.
2. MULTIPLE (LYMPH NODES)
   - a. *Specific*: Infectious mononucleosis, measles, sore throat, tuberculosis, syphilis.
   - b. *Non-specific*: Septicemia, reticuloses.
   - c. *Neoplasms*:
     - i. Primary: Lymphogranuloma, Hodgkin's disease, leukemia.
     - ii. Metastatic: breast, lung, prostate, gastrointestinal tract.

REFERENCE: Dr. Tovee's "Rat Race" Apr. 1957.

FIGURE 2. Prehn's sign states that elevation of the scrotum gives relief of pain in epididymitis, but usually does not ease the pain in torsion of the testicle. Thus, this elevating adhesive support confirms our diagnosis of inflammation of the epididymis.

This condition came on suddenly (over a period of twenty-four hours) and was accompanied by fever (104° F), chills and leukocytosis. The tender red oedematous scrotum has acute local pain which may be referred to the inguinal region with such severity that it simulates acute appendicitis.

The condition follows genito-urinary operations or long term catheterizations. The infection can be blood borne as in septicemia from a focus anywhere in the body. Lymphatic spread also occurs, but the most common form is direct extension from an infection in the prostate or seminal vesicles. This was previously gonorrheal, but now B. Coli, Staphylococcal or Streptococcal are the most common organisms. Treatment consists of complete bed rest until the acute inflammation subsides with scrotal elevation and local heat plus antibiotics.

Prophylactic ligation of the vas deferens in prostatic surgery has decreased the incidence.

Differential diagnosis of lumps in the scrotum: remember that you can't get above an indirect inguinal hernia!

TISSUE	CONGENITAL	TRAUMATIC	INFLAMMATORY	NEOPLASTIC
1. Scrotum			Secondary to general disease Chemical agents Elephantiasis	Lipoma Fibroma Carcinoma (coal tars)
2. Testicle	Fusion Polyorchidism	Orchitis Torsion	Secondary to general infection Mumps Secondary to epididymitis Gumma	Seminoma Teratoma Embryonal carcinoma Chorion-epithelioma
3. Epididymis	Cyst Spermatocele		Non-specific Gonorrheal Secondary to prostatitis Tuberculosis Kidney abscess Precipitates hydrocele	Solid tumours 60% benign 40% carcinoma
4. Tunica Vaginalis	Hydrocele Hematocele Aneurysm	Precipitates hydrocele	Precipitates hydrocele Chylocele	Fibroma Lipoma

REFERENCE: FLETCHER H. COLBY, Essential Urology, 3rd Edition 1956.

FIGURE 3. The Stryker frame or "Stryker" as it is more commonly called is a modification of the Bradford frame which allows a patient to be turned with ease by two nurses instead of two orderlies, a nurse, a medical student and an interne. It is used extensively on neurological wards where paraplegics are turned hourly or two hourly to prevent bed sores.

Anterior and posterior frames are covered with canvas and fit on a pivot device. The patient can be maintained in perfect posture for spinal fractures or fusions and still be comfortable. A writing table and facilities for a bed pan and traction are built in. The frequent turning prevents: decubitus ulcers, gastrointestinal disturbance, pulmonary emboli, post-operative pneumonia, and renal calculi.

REFERENCE: Sister Angeline at St. Michaels hospital provided several commercial articles.

FIGURE 4. This is balanced traction with a large Balkan beam stretching over the bed suspending a Thomas Splint with slings. There is a Pearson flexed-knee attachment on the splint. A Kirshner wire with a Zimmer wire spreader is inserted in the upper end of the tibia, and the apparatus is suspended by pulleys and weights, thus permitting comfortable relaxation of the knee joint while traction of the fractured femur is maintained. This also allows the patient to move about in bed.

The principle is one of counter balance between a weight on the broken limb and the sliding weight of the body because the foot of the bed is raised on blocks. The cord attached to the stirrup and spreader is passed directly over a pulley at the foot of the bed with a weight of ten pounds or more suspended from it.

Note also the attachment that keeps the foot in dorsiflexion and thus prevents shortening of the Achilles tendon. This enables the patient to exercise the leg and walk normally with minimal rehabilitation.

REFERENCE: WATSON-JONES, Fractures and Joint Injuries, Vol. II, 4th Edn.

ACKNOWLEDGEMENT

The editors wish to thank Mr. Arthur Smialowski and Miss Marilyn Bliss of St. Michael's Photography Department for supplying the pictures.

We are also grateful to Drs. Horsey, Moffat, Van Patter, Shannon, Russell and Tovee for their valuable suggestions.

ABSTRACTS

R. F. ARMSTRONG, 5T9

Differential Diagnosis of Congenital Heart Disease in Infancy: B. G. Wendum, Journal of the American Medical Association, **165**: 651, 1957.

Study of the differential diagnosis of congenital heart disease should only be based on evidence from autopsy or operation. This article is based on 279 autopsy reports.

By using an accurate history, careful physical examination, X-rays, fluoroscopy, and electrocardiograms the following points should be considered:

(1) Enlargement of chambers, presence of both ventricles and both atria, single ventricle, inversion of cardiac chambers.

(2) Presence, enlargement, and position of great vessels and their branches.

(3) Systemic venous return.

(4) Pulmonary venous return.

(5) Arteriovenous shunt.

(6) Venous atrial shunt.

(7) Congestive failure.
(8) Cerebral anoxemia.
(9) Blood supply to body.
(10) Blood supply to lungs.
(11) Heart murmur.

The main operable malformations giving difficulty in the first month are: (1) transposition of the great vessels, (2) preductal coarctation, (3) pulmonary stenosis, (4) drainage of all pulmonary veins into the right atrium, (5) vascular ring. Difficulty developing later is usually due to various shunt lesions including patent ductus arteriosus, atrial and ventricular septal defects, endocardial fibroelastosis and anomalous origin of the left coronary artery. A complete truncus arteriosus cannot be treated surgically.

An accurate diagnosis of congenital heart malformations in infancy will allow such children to be sent to a centre where the facilities and personnel are available for treating these defects.

Sudden Death from Coronary Atherosclerosis: David M. Spain and Victoria A. Bradess, Archives of Internal Medicine, **100**: 228, 1957.

This study consists of a group of 1,109 cases of sudden death from coronary artherosclerosis occurring consecutively in one community.

Age: Although the greatest incidence was in those over 55, comparison with earlier studies showed an increase in those below 55 in the past few years.

Sex: Below the age of 55, the incidence in women was much less, but above this age it approaches the incidence in man. As the age increases the ratio of male to female changes from 12 : 1 to 2.5 : 1. It is believed that this difference is partly explained on an endocrine baxsis.

Race: In this study the incidence in 65 negro cases had the same distribution as in the white cases. Other studies have shown a lower incidence in the negro, but further data is necessary in order to determine whether this is due to dietary factors or an inborn immunity in the negro.

Physical Activity: The occupations were classified as: (1) sedentary, (2) moderate activity, and (3) strenuous activity. Below 55, the incidence was much greater in the sedentary group than in the active group. Economic status did not seem to be a factor, but more study is required to determine the cause of this difference.

Physical exertion preceding death occurred only in a small number, and did not appear to be a factor.

Alcoholism: The incidence in the 60 alcoholics in this group did not significantly differ from the whole group Alcoholism does not seem to alter the atherogenic process.

Treatment of Cerebrovascular Conditions in the Elderly: J. G. Pincock, Canadian Medical Association Journal, **77**: 25, 1957.

With the rise in the incidence of cerebrovascular accidents within the past years, treatment which will restore maximum function has become increasingly important. In this series of 117 patients the rehabilitation was divided into three phases:

1. In the first 48-hour period diagnosis and general assessment of the patient were carried out.
2. Following the initial period, a programme of passive and active physiotherapy was started with special attention to foot drop, weakness of hands, and aphasia.
3. With the onset of severe spasticity six to eight weeks after the attack, physiotherapy and recreation were continued and social rehabilitation begun.

The results of this study were as follows:

1. The improvement obtained was usually maintained for several years.
2. Mortality in this group was similar to that of normal people in the same age range. Recurrences occurred in 17 cases, usually within two years.

This form of management seems to be the most effective way of obtaining satisfactory results.

Prognosis of Subarachnoid Hemorrhage. A Comparison Between Patients with Verified Aneurysms and Patients with Normal Angiograms: G. Bjorkesten and Henry Troupp, Journal of Neuro-surgery, **434**: 14, 1957.

For this study patients were divided into two groups:

1. Aneurysm Series: 40 patients with aneurysms confirmed by angiography or autopsy.
2. Non-aneurysm Series: 61 patients with subarachnoid hemorrhage verified by lumbar puncture, but with normal bilateral carotid angiograms.

These patients were all treated conservatively. The morality rate in the aneurysm series was ten times that of the non-aneurysm series. Aneurysms of the internal carotid artery had the worst prognosis, and of the anterior cerebral artery, the best.

Possible causes for hemorrhage in the non-aneurysm series were:

a. Aneurysm not seen in angiogram.
b. Spontaneous thrombosis of small ruptured aneurysm.
c. Angiomatous malformations.
d. Telangiectasis.

The prognosis for patients with subarachnoid hemorrhage is much better if the angiograms are normal.

The Clinical Investigation of Pacatal in Open Psychiatric Settings: G. J. Sawrer-Foner and E. K. Koranyi, Canadian Medical Association Journal, **77**: 450, 1957.

The commercial drug "Pacatal" was used in the treatment of psychiatric patients. In sufficient dosages it was found to reduce the energy output in overactive patients making them feel calm and sedated. It also produced a certain degree of hypnosis in most patients. No serious toxic effects were found, but patients being treated should be kept under proper supervision. Most of the side effects were due to its atropine-like actions, and there was also a tendency for a slight elevation of the white blood cell count. In this series "Pacatal" was a beneficial and relatively safe drug in the treatment of certain types of psychiatric illness.

BOOK REVIEWS

THE CENTURY OF THE SURGEON. Jurgen Thorwald, 1956; 390 pp., Illust.

In this book the momentous surgical advances of the 19th century are described through the eyes of a young physician who ages with the century.

The story revolves upon the discovery of anaesthesia. The personal, political and legal intrigue surrounding this discovery is told in vivid detail as the trio of discoverers fought for fame and even fortune. In numerous flashbacks, the horrors of surgery without anaesthesia are recounted.

National prejudice, inherent in this type of writing, has been virtually banished.

Many of the proper names which harass students because they "have no meaning" take on new significance as the famous figures are described as they lived and practised.

This book can be appreciated by all.

from the premedical student to the practitioner.

FOR FUTURE DOCTORS, Alan Gregg, M.D., University of Chicago Press, 1957, 165 pp.

This book is a collection of eleven addresses delivered by the late Dr. Gregg at various medical commencements.

He speaks of responsibility, creativeness in medicine, language, incompleteness and humility, emergent ability, medical institutes and travel.

Such statements as " . . . if you wrote a history that satisfied *you* it would be a good history" and "patients do not want . . . mere Quiz Kids—persons as miraculous mentally as they are immature in every other way" may meet with either agreement or disagreement, but by their very nature they must be met with thought. And this book is literally full of such thought-provoking statements.

That there is more, much more, to being a doctor than the mere degree of M.D. is the basic theme running consistently through the varied topics of these essays.

These thoughts are probably best directed at the graduating medical student—to whom Dr. Gregg first addressed them—for it is they, more than any other persons in the profession, who are preoccupied with textbook knowledge, and who have lost sight of or have never seen the values as set forth in this book.

A.C.S.

For the Aged and Senile Patient

ORAL *Metrazol*

— to help the geriatric patient with early or advanced signs of mental confusion attain a more optimistic outlook on life, to be more cooperative and alert, often with improvement in appetite and sleep pattern.

METRAZOL, a centrally acting stimulant, increases both respiratory and circulatory efficiency without overexcitation or a hypertensive effect.

Dose: 1½ to 3 grains, 1 or 2 teaspoonfuls Liquidum, or the tablets, every three or four hours.

Metrazol tablets, 1½ grs. (100 mg.) each. Metrazol Liquidum, a wine-like flavored 15 per cent alcoholic elixir containing 100 mg. Metrazol and 1 mg. thiamine HCl per teaspoonful.

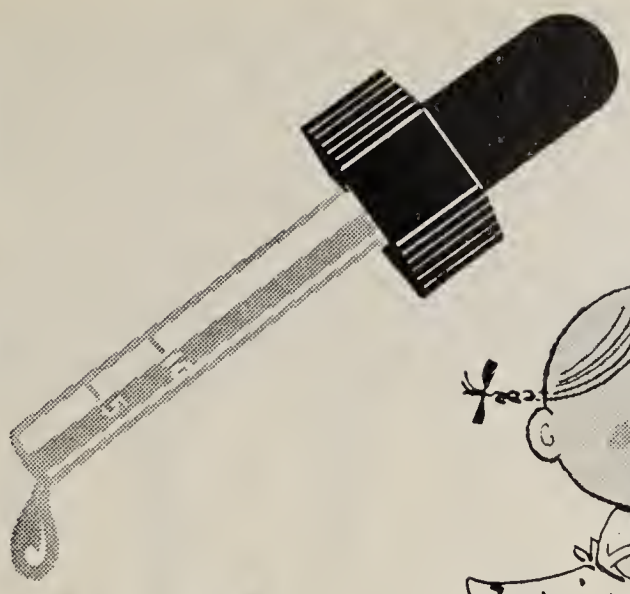
Metrazol Liquidum — pints

Metrazol tablets — 100's, 500's

Metrazol, brand of pentylenetetrazol, Trademark reg., E. Bilhuber, Inc.; marketed by Bilhuber-Knoll Corp., Orange, N. J.

MERCK & CO. Limited *exclusive distributor*

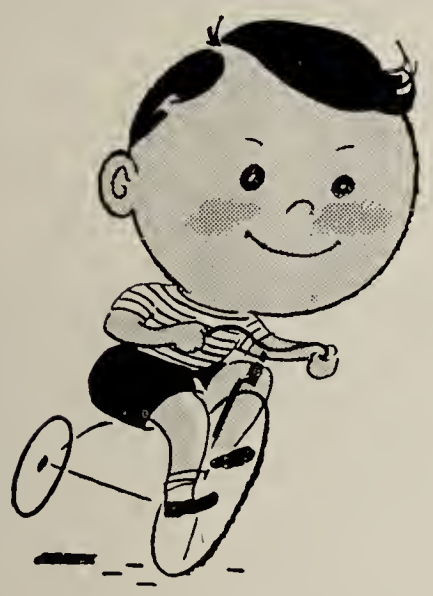
MONTREAL TORONTO VANCOUVER VALLEYFIELD



MULTI-VITAMINS

for infants and children

CONVENIENT, ECONOMICAL, PLEASANT-TASTING



"Ostoco" BRAND DROPS

The unique formulation accounts for the freedom from the relatively disagreeable taste of other drop-dose preparations. Children of all ages welcome these agreeably flavoured drops whether given directly on the tongue or mixed with the feeding formula, fruit juices or other liquids.

Each 5-DROP DAILY DOSE (0.25 cc.) contains:

VITAMIN A	2000 Int. Units
VITAMIN D	1000 Int. Units
VITAMIN C	30 mg.
VITAMIN B_1	1 mg.
RIBOFLAVIN	0.6 mg.
NIACINAMIDE	4 mg.
PYRIDOXINE HCl.	0.05 mg.
SODIUM IODIDE	0.04 mg.

Water-dispersible

MODES OF ISSUE

8 cc. 32 days' supply
15 cc. 60 days' supply
30 cc. 120 days' supply

COST PER DAY

3½ to 4½ cents depending on size of bottle.

Dose for dose, these vitamin drops cost the patient less

Charles E. Frosst & Co.
MONTREAL CANADA

when corticosteroids are indicated...

prescribe

PARACORT*

PREDNISONE, PARKE-DAVIS

or

PARACORTOL*

PREDNISOLONE, PARKE-DAVIS

three to five times the activity of
cortisone or hydrocortisone

supplied: PARACORT and PARACORTOL are available as 5 mg. and 2.5 mg. scored tablets, bottles of 30 and 100

MEDICAMENTA VERA

PARKE-DAVIS

PARKE, DAVIS & CO., LTD. • TORONTO 14, ONTARIO

*TRADE MARK

50151

CONSIDER THE HUSBAND

"THE PRESENCE OF TRICHOMONADS in the male genitourinary tract should always be suspected in the husband of a woman who is repeatedly reinfected."[1] Instead of merely suggesting that the husband use a sheath to prevent re-infection of the patient with vaginal trichomoniasis, many physicians specify RAMSES prophylactics in writing. Being specific not only saves the patient from embarrassment but ensures husband cooperation. Most of them know and prefer RAMSES.

Transparent, tissue-thin and smooth, yet strong, RAMSES natural gum rubber prophylactics are *different*. RAMSES are prophylactics with "built-in" sensitivity. Their acceptability and high quality ensure the protection that is the very foundation of re-infection control.

1. Draper, J. W.: Internat. Rec. Med. *168*:563 (Sept.) 1953.

RAMSES*

prophylactics

*Trademark

JULIUS SCHMID (Canada) Ltd.
32 Bermondsey Road, Toronto 16, Canada